Département virologie

Rapport Hcéres

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

Research Units Department

AERES report on unit:

Department of Virology

Under the supervision of the following institutions and research bodies:

INSTITUT PASTEUR

INSERM

CNRS

Paris Diderot University

March 2012

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

Section des Unités de recherche

Le Président de l'AERES

Didier Houssin

Section des Unités de recherche

Le Directeur

Pierre Glaudes

Unit

Name of unit:	Department of Virology
Acronym of unit:	
Label requested:	Departement (Institut Pasteur, Université Paris Diderot)/UMR_S/UMR
Present no.:	
Name of Director (2009-2012):	Mr Félix REY
Name of project leader (2013-2017):	Mr Olivier SCHWARTZ

Members of the committee of experts

Chair:	Mr Winfried WEISSENHORN, Grenoble
Experts:	Mr Charles BANGHAM, London, United Kingdom
	Mr Stephan BECKER, Marburg, Germany
	Mr Serge BENICHOU, Paris (Inserm CSS5 representative)
	Mr Dieter BLAASS, Vienna, Austria
	Mr Esteban DOMINGO, Madrid, Spain
	Mr Richard M. ELLIOT, St-Andrews, United Kingdom
	Mr Lynn ENQUIST, Princeton, USA (Pasteur Institute scientific council representative)
	Mr Hans-Dieter KIENK, Marburg, Germany
	Mr Mark MARSH, London, United Kingdom
	Ms Jane A. MCKEATING, United Kingdom
	Mr Thomas MICHIELS, Louvain, Belgium
	Mr Michel NUSSENZWEIG, New York, USA (Pasteur Institute scientific council representative)
	Ms Hanneke SCHUITEMAKER, Amsterdam, The Netherlands
	Mr Cameron SIMMONS, Oxford, United Kingdom
	Mr Ian TAYLOR, Mill Hill, United Kingdom

Representatives present during the visit

Scientific Delegate representing AERES:

Mr David DOMBROVICZ

Representatives of the unit's supervising institutions and bodies:

Ms Christine CIERICI, Paris Diderot University

Ms Evelyne JOUVIN-MARCHE, CNRS

Ms Christine TUFFREAU, Inserm

Report

1 • Introduction

Date and conduct of visit:

The visit took place from March 4th to 7th 2012 and was carried out by an international team of 17 scientists with complementary expertise in the research areas of the 19 teams that were evaluated. The visit started with general introductions by the Director General and by the Scientific Director of the Pasteur Institute. This was followed by an overview of the past achievements presented by the Department Head, who will be stepping down as head of the department. The designated future head of the department subsequently presented the overall future scientific direction of the department.

The review committee was then split into two subcommittees in order to attend the presentations and discussions of the 19 heads of team. Each ~25-30 min presentation was followed by 20-25 min discussion. The presentations and discussions of three junior groups were limited to 35 minutes. In addition, the head of the Pathodisc platform presented his work and future plans to subcommittee 1 in a 15 minutes presentation. On Monday committee members split into three subgroups and met separately for ~ 55 minutes with staff scientists, engineers and technicians, and students and postdocs.

Following the team presentations on Tuesday the committee met with the current and designated head of the department and the Scientific Director of Pasteur Institute to discuss and clarify department issues. The committee then met in the afternoon of March 6th to establish the present report.

History and geographical location of the team, and overall description of its field and activities:

The Department of Virology is part of the Institut Pasteur (Paris). It is currently composed of 19 teams, some of which have one or several sub groups. The research activities cover most aspects of virology as well as immunological aspects including vaccine design. The current research focus of the department is on retroviruses including HIV and HTLV, Arboviruses (Flaviviruses, Alphaviruses, Bunyaviruses), Influenza virus, SARS, HBV, Hepacivirus (HCV, GBV-B), Papillomaviruses, Rabies virus and enteroviruses. Different aspects of HIV and Arboviruses are covered across several teams.

Severa teams host National Reference Centers (NRC) and/or are WHO Collaborating Centers (WHO reference laboratory for SARS and H5 influenza viruses) for influenza virus (Team 16), papilloma viruses (Team 6), arboviruses (Teams 5 and 15), viral haemorrhagic fever (Team 15) and enteroviruses (Team 4).

Two teams are affiliated with Inserm and 6 teams with the CNRS. One team is affiliated with the University Paris Diderot.

One team is located at the Lyon Gerland campus in close proximity to the P4 Laboratory.

Management team:

Department head has directed the department since 2004, and will step down at then end of 2012. The new designated director of the department will take over on January 1st, 2013. A scientific council, which includes members from each team of the department supports management.

Unit workforce:

Workforce	Number on 06/30/2011	Number on 01/01/2013	2013-2017 Number of producers**
N1: Professors or assistant professors	7	6	6
N2: EPST or EPIC researchers)	19	19	18
N3: Other professors and researchers	68	46	38
N4: Engineers, technicians and administrative staff *on a permanent position	75 (56,9)	68 (51,3)	
N5: Engineers, technicians and administrative staff * on a non-permanent position	9 (8,5)		
N6: Postdoctoral students having spent at least 12 months in the team	79		
N7: Doctoral students	39		
N8: PhD defended	54		
N9: Number of Habilitations to Direct Research (HDR) defended	14		
N10: People habilitated to direct research or similar	46	44	
TOTAL N1 to N7	**296 (276,4)**	**139 (122,3)**	**62**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:

http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-teames-de-recherche/Principes-d-evaluation.

2 • Assessment of the unit

Overall opinion on the unit:

The Department of Virology was considered to be an excellent department with a few outstanding teams, including the team headed by the head of the department. The department also succeeded to attract two junior group leaders (Teams 12 and 17) bringing new innovative projects that are complementary to the ongoing science in the department. Moreover, these new groups have already made excellent to outstanding contributions to their respective fields. The installation of a new group for arboviruses (Team 19) was considered to be an excellent choice to maintain the important existing expertise.

Overall the department is impressive with regard to the wide range of topics in virology and its exceptionally broad expertise from vaccinology to structural biology. While many teams make excellent contributions, a minor number could improve their scientific output given the very significant investment of Pasteur Institute in the support of the teams.

Numerous fruitful collaborations across teams exist. Notably, the Chikungunya virus initiative is an excellent example for efficient collaboration both within and across Pasteur departments. These collaborations produced a high number of common publications some with excellent and outstanding impact. Thus the Chikungunya virus initiative highlights the unique strength of the department that is largely based on the complementary expertise of the teams.

Strengths and opportunities:

- There is depth and breadth in the research topics of the department
- The department hosts an outstanding structural biology team
- Teams run excellent programs on arboviruses, HIV, papilloma viruses, enteroviruses
- There is flexibility to recruit young group leaders with attractive start-up packages that will bring in new expertise
- There is an excellent capacity to attract industrial funding
- The campus offers high capacity for translational research
- The department has a privilegded access to biological material via the reference centers

Weaknesses and risks:

- The unique size of the department and the range of interests of the future team heads represents a significant challenge to manage and lead such a department
- The unique size and range of interests within the department pose a challenge to focus the resarch activities
- Several projects depend on access to adequate biosafety facilities, which poses a challenge for future research
- Interactions across teams could be increased
- There is a limited integration of the department with the international Institut Pasteur network (IP network).
- Many external funding sources end in 2012.
- The research on hepatitis is scattered across three different teams.

Recommendations:

- Focus the future research initially on 3 topics and potentially extend later
- Identify common interests for a new project and launch a new Chikungunya-like task force across the department and Pasteur Institute
- Regrouping of the hepatitis research effort into one team would be beneficial
- Seek more active collaborations with respect to training and research programs with the international Pasteur network.
- Focus on external funding to keep up the excellent scientific production.
- Install a career development program for post docs and foster mentoring of PhD students
- Increase the number of staff producers.

3 • Detailed assessments

Assessment of scientific quality and production:

The research carried out at the virology department is highly relevant and original. It focuses on a number of important topics in virology, notably the biology and pathology of newly emerging viruses with a unique focus on arboviruses, the relationship between viruses and cancer and the development of new vaccines employing viral vectors. The quality of research is in many aspects outstanding or excellent thus leading to a high impact within the scientific community. Notable are outstanding contributions from the Structural Virology team on the mechanism of viral entry machines, from the Molecular Retrovirology team on viruses and cancer, from the Viruses and RNA Interference team on antiviral immunity in drosophila and from the Viral Populations and Pathogenesis team on virus evolution and fitness. Many other teams including the Regulation of Retroviral Infections team, the Virus and Immunity team, the Genetics, Papillomavirus and Human Cancer team, the Biology of Enteric viruses team, the Molecular Genetics of RNA Viruses team, the Oncogenic virus Epidemiology and Pathophysiology team and the Viral Pathogenesis team contributed to the excellent output of the department.

The department published in total 603 papers including manuscripts in very high or high profile journals such as Nature, Science, Nature Immunology, Nature Medicine, Nature Methods, PLoS Medicine, Cell Host & Microbe, Journal of Experimental Medicine, PNAS, EMBO Journal, Blood, PLoS Pathogens…

54 PhD students defended their thesis, which is an excellent average of ~3 theses per team.

The number of 38 producers compared to 46 staff (in 2003) signals out a total of 8 non-producers. However, this seems to be largely due to the fact that it includes recently hired researchers (between 2009 and 2011) who have not yet published 4 papers from the team. It also reflects the expected departure of staff between 2011 and 2013.

Assessment of the team's integration into its environment:

The department has an excellent valorization record. A total number of 30 patents has been obtained and a number of these have been licensed to industrial partners. Most active in obtaining patents are teams E14, E3, E5 and E11.

One startup Pasteur-based biotech company was founded in 2010.

Institut Carnot grants were obtained by the Hepacivirus and Innate Immunity teams, Pathogenesis of Hepatitis B virus team and Viral Genomics and Vaccination team.

External funding of the department was excellent for most teams with funding from national sources and many European contracts. A number of ongoing contracts will terminate in 2012 and the teams will have to ensure continuity in external funding. Two young teams secured highly prestigious ERC young investigator grants.

The department has an excellent visibility within novel activities of innovation clusters.

The Regulation of Retroviral Infections team participates in the Labex "Vaccine Research Institue", the ANRS Coordination of HIV/AIDS programs in Cambodia and Vietnam and in the ANRS Cohort on HIV Controllers.

Labex "IBEID" participating teams include Structural Virology, Virus Epidemiology and Pathophysiology, Viruses and RNA Interference, Virus and Immunity, Viral Population and pathogenesis, Arboviruses and Insect Vectors, and Molecular Genetics of RNA Viruses.

Assessment of the research team's reputation and drawing power:

Team members received numerous prestigious awards. Most notable is the recognition of the work of the head of the Regulation of Retroviral Infections team, by the award of the Nobel Prize in Medicine and her election into the French National Academy of Sciences. The head of the Structural Virology teams was elected a member of the Acadaemia Europea, the European Academy of Microbiology, the French National Academy of Sciences and received the Rene & Andre Duquesne award. The head of the Infection and Immunity team was elected an EMBO member and received the Louis Tartois award from FRM. The head of the Oncogenic Virus and Epidemiology and Pathophysiology team was elected member of the National Academy of Medicine and one team member received the award from the National Academy of Medicine. The head of the Molecular Retrovirology team was elected a member of the Academia Europea. Two members of the Regulation of Retroviral Infectiosns team obtained the Line Renaud award from FRM. The head of the Molecular Virology and Vaccinology team obtained the Grand Award from FRM.

Most teams participated actively in international and national conferences through invitations.

A number of teams are successfully recruiting researchers, post docs and students from abroad. An International Pasteur Institute PhD program could increase the attractiveness of the departments for national and foreign students. There is a striking lack of PhD students or scientists from countries where the IP international network has a presence. This would seem an obvious way to forge closer collaborative links with the IP network and the enviable scientific opportunities this could bring.

Multiple national and international collaborations are listed for the different teams. Collaborative projects are highlighted by many collaborative grants such as ANR involving few groups on a national level and European contracts involving a larger number of participating groups.

Assessment of the team's governance and life:

Department management is supported by the Scientific Council of the department that participates in decision making. The department also gets feedback from the Scientific Director of Pasteur Institute. The department's interests are represented in the Scientific Council of the Pasteur Institute; one team head is member of the Scientific Council (Team 13 head in the past and currently Team 7 head).

The award of the Nobel Prize in Medicine to Team 2 head was an excellent advertisement for the Pasteur Institute and provided a unique extended international visibility.

External communication was further fostered by many interviews (TV, radio, newspapers) given by the PI of the Viruses and Immunity team.

The technical staff (engineers and technicians) raised some concerns about their future with regard to the planned overall reduction of technical personnel. Furthermore the evaluation criteria for promotion including authorship policy might benefit from some clarifications.

The department is ready to take risks in addressing the problems linked to emerging viruses. It has the impact to stimulate innovative research across disciplines on emerging pathogens. An excellent example is the chikungunya virus initiative.

The department meets on a yearly basis for a retreat that fosters talks by students, postdocs and staff. Since last year the retreat is held outside the Paris Pasteur Institute facilities, which allowed for a more active participation of the entire department.

Members of the department are involved in the yearly oragnization of the "Journées Francophones de Virolgie" at Pasteur Institute (Biology of Enteric Viruses, Antiviral Strategies and Biology of Enteric Viruses teams).

Assessment of the strategy and 5-year project:

The department has a much-appreciated feasible and long-term strategy that builds on its current strengths. Its future focus will be on arboviruses and the impact of climate change, viruses and cancer, vaccines and anti-viral drugs. Development of two innovative vaccine platforms for prophylactic and therapeutic vaccines will be further pursued.

The budget for the department is split between the teams based on discussions between the head of department and the scientific director of Pasteur Institute.

The projects proposed for the next five years are a good balance between feasible and high-risk projects. Notably all vaccine development programs are high-risk projects but with enormous socioeconomic potential.

Assessment of the team's involvement in training:

Almost all teams report teaching activities at Pasteur Institute or at universities across Paris:

Team members organize post graduate teaching courses at Pasteur Institute including Fundamental Virology and a course on Zoonosis (Biology of Emerging Infectious Diseases team). They contribute to the Pasteur Asia Virology course (Biology of Emerging Infectious Diseases team; Molecular Genetics of RNA Viruses team) and to university teaching at the L1, L2, L3 and master level at University Paris Diderot and Université Paris Sud (Molecular Genetics of RNA Viruses team), for the virology module at ENS Ulm, Paris and ENS Cachan (Molecular Genetics of RNA Viruses team) and for undergraduate and graduate teaching at Universities Paris V, VI, VII, XI and XII (Molecular Retrovirology team; Regulation of Retroviral Infections team; Structural virology Team; Viral Genomics and Vaccination team; Molecular Genetics of RNA Viruses team).

One team head is director adjunct of the Ecole Doctorale Gc3iD, University Paris Diderot Paris 7 (Molecular Genetics of RNA viruses team).

Department scientists also teach at Pasteur Institute (Paris or Lille), at the University Versaille-Saint Quentin, at ENS Ulm or at the Universities Paris 7 and Paris 11.

54 students have defended their thesis during the review period and 51 of them have published at least one paper (most of them more than 2 papers). Students participate in the "Club Viro" twice per month where they present their results. They also participate in the scientific retreats organized by the department outside the campus. Journal clubs are organized separately by each team.

Students are supervised by a doctoral advisor and by a tutor chosen from another team. PhD students are mainly financed through stipends from the French Ministry of Higher Education and Research (around 60%) and from external grants (ANRS, FRM, Sidaction, EU Marie Curie or other fellowships).

Trainees (master 1 and 2) are hosted by Institut Pasteur within the framework of their studies. An agreement is signed between Institut Pasteur and their university and they receive a monthly stipend of 430 euros.

4 • Team-by-team analysis

Team 1: Viral Pathogenesis

Team leader: Mr Fernando ARENZANA-SEISDEDOS

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors			
N2: EPST or EPIC researchers	3	3	2
N3: Other professors and researchers		1	1
N4: Engineers, technicians and administrative staff * on a permanent position	2 (1,5)	2 (1,5)	
N5: Engineers, technicians and administrative staff * on a non-permanent position			
N6: Postdoctoral students having spent at least 12 months in the team	13		
N7: Doctoral students	1		
N8: PhD defended	3		
N9: Number of Habilitations to Direct Research (HDR) defended	2		
N10: People habilitated to direct research or similar	2	3	
TOTAL N1 to N7	**19**	**6**	**3**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-teames-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

The team works on the mechanisms of chemokine/chemokine receptor interaction, with particular emphasis on chemokine receptors involved in HIV entry. It has had three main components to their work. 1) The role of Gag binding in chemokine presentation. 2) The role CXCR7 as a CXCL12 binder. 3) The role of CXCR4 in the pathology of WHIM syndrome and ICL, and the influence of chemokine receptor binding on HIV transmission.

The in vivo model for CXCL12-GAG binding is perhaps the best model currently available for investigating the role of proteoglycans in presenting chemokines. The model indicates a clear role for CXCL12-GAG binding in blood vessel regrowth after ischaemic injury, and is now ripe for the further investigations discussed below.

The team has made significant insights to the role of CXCR4 and CXCL12 in two pathological situations – WHIM syndromes and idiopathic CD4 T cell lymphocytopenia (ICL). In addition they have identified a second SDF binder, namely CXCR7, which appears to interact with and regulate CXCR4 function. However, these projects were both led by a team member who has now left the Institute.

The team has a long-standing interest and reputation in the analysis of chemokine receptors involved in HIV entry, and it has continued to make interesting observations into CCR5 and CXCR4 function in HIV entry.

In the period 2007-2011, the team published 42 papers (orignal and reviews) in peer reviewed journals of which 10 were primary original research papers (i.e. with team members as first or last author). The leader of the team is a coauthor on 24 papers. Some papers have been published in high impact journals. Two of the scientists that produced papers listed in the review period have left the group.

Assessment of the research team's integration into its environment:

The team has patented CXCL12-gamma and disclosed the invention of an animal model for WHIM syndrome. In the past 5 year period, the team members were not awarded prizes or distinctions. Invitations to international events are not reported. Nationalities of appointed personnel are not given so the committee is unable to judge the ability of the group to recruit students from abroad.

The team has been well supported by external grants, mostly from French agencies, with support continuing through LABEX to 2016. However, the group will need to find additional support this year to ensure it has a sound financial future. The list of financial support does indicate participation in international consortia.

Assessment of the research team's reputation and drawing power:

The team leader is a member of the scientific council of the Belgian FRS/FNRS and the Bettencourt Schueller Foundation and is an evaluator for the ERC. He has also served on a Pasteur Institute and French panels and advisory boards. He received the AIDS Research award from SIDACTION in 2003. A number of meeting abstracts are listed in the publications list and it appears the team leader was invited to several international meetings, as was also the case for one of the staff scientists that recently moved out of the department.

It seems that most of the group members are from France, there is no indication otherwise. The group recently added a staff scientist (INSERM). However, this scientist has had limited productivity over the past period which may be a concern.

From the list of publications it can be seen that the group has international collaborations – but these were not described in any detail.

Assessment of the strategy and 5-year project:

The team will continue to follow the work program it has developed over the last few years. The main focuses will be 1) The role of CCR5 dimerization and interactions with other receptors (in particular CCR2 and CD4) and the role of these interactions in HIV infection. 2) Resistance of R5-tropic HIV-1 to chemokine inhibition and 3) Research on the biological role of chemokine/proteoglycan interactions in vivo. However one of the very interesting programs on WHIM syndrome and ICL has been taken by one of the staff scientists who has left and will no longer be pursued in the team.

With respect to point 1, this has been an ongoing debate in the research field. Although conclusions may come from model experimental systems, relating these to primary cells and HIV infection will be difficult. It is not clear that the team's experimental set-up has advantages that differentiate it from other groups.

With respect to point 2, the team aims to test the hypothesis that chemokines and HIV gp120 target distinct CCR5 conformations. Moreover, this may be linked to G protein engagement of CCR5. This research may provide new insight to the entry of HIV and potentially create new ideas on entry inhibitors. Lack of detail in the experimental descriptions renders difficult for the reviewers to assess the proposed experiments. The notion of using monomeric gp120, then uncertainty about how CD4 is brought into these analyses and the extrapolation from a model system to primary cells, are of concern.

Point 3 is interesting and original and represents the best in vivo model for investigating chemokine presentation by proteoglycans currently available. Although the model has not yet provided clear cut insights to CXCL12/CXCR4 function the proposed experiments on B lymphocyte and plasma cell recruitement are potentially interesting. The model has no relevance for HIV infection but it can be used to investigate West Nile virus infection of the central nervous system. In this respect the group should ensure it has effective collaborations with other flavivirus groups in the department.

Conclusion:

- *Overall opinion on the team:*

The group has a very good production and visibility.

- *Strengths and opportunities:*

The proteoglycan model is a potential strength of the team.

- *Weaknesses and risks:*

The studies on CCR5 dimerization and CCR5-HIV interactions are in a highly competitive field and the team may not achieve priority.

The team has lost two highly productive researchers and, with that, interesting lines of research. It would do well to compensate for this to keep research momentum and critical mass in the team.

- *Recommendations:*

- Prioritize the research goals

- Seek external funding

- Try to replace the researchers that left the team with researchers of equal potential

Team 2: Regulation of Retroviral Infections

Team leader: Ms Françoise BARRE-SINOUSSI

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	1	1	1
N2: EPST or EPIC researchers	3	3	3
N3: Other professors and researchers	3	4	4
N4: Engineers, technicians and administrative staff * on a permanent position	8 (7,5)	8 (7,5)	
N5: Engineers, technicians and administrative staff * on a non-permanent position	1 (0,5)		
N6: Postdoctoral students having spent at least 12 months in the team	8		
N7: Doctoral students	4		
N8: PhD defended	3		
N9: Number of Habilitations to Direct Research (HDR) defended	1		
N10: People habilitated to direct research or similar	6	8	
TOTAL N1 to N7	**28 (27)**	**16 (15,5)**	**8**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-teames-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

The team is active in two extremely relevant fields of HIV research and focusses on the underlying mechanism for the natural control of HIV-1 infection (both in the natural course and after interruption of treatment that was initiated during the acute phase of infection) and on the underlying mechanism of control for abnormal immune activation. For both lines of research, the teams have chosen unique hypotheses and experimental approaches that have already resulted in highly cited publications in journals with high impact factors.

The output of the team is excellent, both in quantity and quality. The team has contributed to a total of 63 articles, of which 38 are primary papers, that were published in peer reviewed journals.

Assessment of the research team's integration into its environment:

The team filed three patents, which should be considered an excellent achievement. The head of the team is supervising research activities in Vietnam and Cambodia funded by ANRS. The team is participating in the ANRS cohort studies on HIV controllers. The funding from external sources has been excellent and it may be expected that the team should be able to continue to find funding for their research. All funding comes from French organizations, no record of funding from international organizations. The launch of the LABEX Vaccine Research Institute for which the head of the team will serve as Honorary President, will be a major achievement further fuelling the research opportunities of this team.

Assessment of the research team's reputation and drawing power:

The team leader was awarded the 2008 Nobel Prize for Medicine for the discovery of the human immunodeficiency virus. She also is a member of a number of national and international committees, boards and councils (French Academy of Sciences, EMBO, Scientific Board of the Global HIV Vaccine Enterprise, President-elect of the International AIDS Society), Doctor Honoris Causa of 7 universities (inc. Lund, Tulane, Brussels). She has been invited as a special guest to give 63 lectures all over the world (inc. United Nation General Assembly Special Session, 2011 Burnett Oration Melbourne, 2011 Claude Bernard Lecture at the Royal Society) and 25 keynote lectures at the opening, closing and/or special sessions of International Conferences (inc. ICAAC 2009, IUMS 2011, ESPID 2011)

The other PIs of the team have been invited as speakers in 14 international conferences including the Gordon Research Conference, Keystone Symposia and International AIDS Society Conferences. They are or have been members of many evaluation committees for Afssaps, AERES, Fondation de France, German Federal Ministry of Research programs Forsys & e:bio, Specialized Scientific Committees (CSS) for ANRS, International symposium on natural immunity to HIV and others. Two team members received the French Foundation for Medical Research (FRM) Award for AIDS research in 2008 and 2010, respectively.

From the list of publications it can be extracted that members of the team are involved in national and international collaborations.

Assessment of the strategy and 5-year project:

The team will continue their research into the natural control of HIV-1 infection and the underlying mechanism for prevention of hyper-immune activation that is the driver of disease progression in pathogenic SIV infection and HIV infection in humans. The interest and expertise of the team in innate immune factors, which might be critical in the pathogenesis of HIV infection and vaccine efficacy is extremely valuable. Taking this approach, they have created themselves a unique position in a highly competitive field. Their approach will further contribute in a unique way to the LABEX Vaccine Research Institute.

Conclusion:

- *Overall opinion on the team:*

The team has performed extremely well and shows excellent ideas for the continuation of their research. The head of the team has created an atmosphere of scientific freedom for the team members. The topics of research in the team are coherent but the different members have their own niche and scientific identity.

- *Strengths and opportunities:*

The angle of innate immunity in the approach of unraveling the underlying mechanism for natural control of HIV-1 infection and prevention of hyper-immune activation is original and will provide the team with a unique position in the field.

- *Weaknesses:*

The retirement of the head of the team and of one of the staff scientists will be a challenge for the scientists in the current team.

- *Recommendations:*

Project leaders have shown evidence of being capable of doing independent research. Important expertise and research highly compatible with the interests of the department should be secured.

Team 3: Molecular virology and Vaccins

Team leader: Mr Pierre CHARNEAU

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors			
N2: EPST or EPIC researchers	3	2	1
N3: Other professors and researchers	2	2	1
N4: Engineers, technicians and administrative staff * on a permanent position	1	1	
N5: Engineers, technicians and administrative staff * on a non-permanent position	3		
N6: Postdoctoral students having spent at least 12 months in the team	5		
N7: Doctoral students	1		
N8: PhD defended	1		
N9: Number of Habilitations to Direct Research (HDR) defended	1		
N10: People habilitated to direct research or similar	2	2	
TOTAL N1 to N7	**15**	**5**	**2**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-teames-de-recherche/Principes-d-evaluation.

Detailed assessments

Assessment of scientific quality and production:

Between 2007 and 2011, the team developed very original scientific projects, regarding aspects of both basic HIV-1 replication and translational research using lentiviral vectors for gene therapy and vaccinology. These projects focused on 3 main axes:

1) The molecular virology projects focused on the molecular characterization of mechanisms involved in the early steps of the HIV-1 life cycle (reverse-transcription, intracellular routing of the viral genome leading to uncoating and nuclear import of the viral DNA).

2) The vectorology projects employed lentiviral vectors for the development of potential gene therapy approaches for genetic diseases and HIV infection.

3) The vaccinology projects also used lentiviral vectors for efficient transduction of dendritic cells in order to stimulate a prolonged antigen presentation using this original approach.

The work was mainly performed by postdoctoral fellows and some of the permanent scientists of the team.

Development of these projects produced 23 original publications, with 6 signed in main positions by people from the team; these 6 publications were published in very good journals, including Mol Ther, EMBO J, Methods Mol Biol, JVI, Blood, Retrovirology and J Cell Biol.

Assessment of the research team's integration into its environment:

The team developed a strong valorization activity with 7 international patents licensed to Biotech companies, including the one founded by the head of the team, which is registered since 2007. This excellent capacity to develop translational research projects is certainly one of the strengths of the team. The team head and some other permanent scientists also showed a high ability to obtain external funding from several french funding agencies.

Assessment of the research team's reputation and drawing power:

The team head and some of the permanent scientists have a very good international standing and recognition.

The team head succeeded in the recruitment of very good and productive researchers including postdoctoral fellows and permanent scientists. However, it is also very important to note that only one PhD thesis was defended in the team since 2007. This situation is certainly related to the fact that only one permanent scientist obtained the authorization ("HDR") to manage PhD students from the university. It is planned that the team head will get this authorization from the university in March 2012.

The international visibility of the team might be limited because only one permanent researcher had the opportunity to present his results at international meetings.

Assessment of the strategy and 5-year project:

In total continuity with the nice results and high expertise developed during the last years, the team head and staff scientists will develop original projects focused on the 3 main axes mentioned above: 1) Molecular characterization of the reverse-transcription and pre-integration complexes (RTC and PIC, respectively) of HIV-1 required for the early steps of the virus life cycle; 2 and 3) development of original methods for using lentiviral vectors for gene therapy of HIV-1-infected people with lymphomas or genetic diseases (2), and innovative vaccine strategies for prevention of HIV infection and malaria (3).

While the experimental strategy proposed to elucidate the mechanisms governing intracellular routing of the RT and PIC complexes could be adapted to more relevant natural cell targets of HIV-1, the other projects on vectorology and vaccinology should result in improvement of lentiviral vectors for gene therapy and vaccine development against several pathogens.

Conclusion:

- *Overall opinion on the team:*

In conclusion, the team developed, as evidenced by the good scientific production, original publications and international patents, and will certainly continue to develop original research projects located at the interface between basic science and translational research. The strengths and opportunities of the team are related to the high expertise and the leading position developed since a long time on lentiviral vectors for gene therapy and vaccinology.

- *Strengths and opportunities:*

- The team projects have a very good potential for translational research
- The team has an excellent expertise on the manipulation of lentivirus vectors

- *Weaknesses and risks:*

- One staff member will leave in 2012;
- It is not clear how the project led by the team member who left the team will continue in the lab
- The team head does not hold yet HDR, which means limited access to PhD students

- *Recommendations:*

- Improve the visibility of the team at international meetings
- Pursue training of PhD students

Team 4: Biology of Enteric Viruses

Team leader: Mr Francis DELPEYROUX

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors			
N2: EPST or EPIC researchers	1	1	1
N3: Other professors and researchers	1	1	1
N4: Engineers, technicians and administrative staff * on a permanent position	5 (4)	5 (4)	
N5: Engineers, technicians and administrative staff * on a non-permanent position			
N6: Postdoctoral students having spent at least 12 months in the team	3		
N7: Doctoral students	4		
N8: PhD defended	2		
N9: Number of Habilitations to Direct Research (HDR) defended			
N10: People habilitated to direct research or similar	2		
TOTAL N1 to N7	**14 (13)**	**7 (6)**	**2**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-teames-de-recherche/Principes-d-evaluation.

Detailed assessments

Assessment of scientific quality and production:

The team covers two different aspects of research: one is mainly centered on routine surveillance and detection of new vaccine-derived enterovirus recombinants and the other is basic research aimed at understanding the principles underlying the emergence of new enterovirus variants and the mechanisms of host-virus interactions on the molecular level. The first one lacks originality, but is of imminent importance within the frame of poliovirus eradication, reappearance, and prevention of spread. The second one is of high scientific quality. The collaborations with the international Institut Pasteur network are very important for both tasks as they allow easy and rapid access to emerging viruses for investigation. The combination of these two aspects has yielded important results. Considering that the routine part of the work might be considerable, the output in terms of publications is high. In general, the topic is of high scientific interest and the research of very good quality.

Considering the small size of the group (currently 2 staff scientists, 3 until the retirement of one team member in 2010), the publication record is high. The group has published 35 papers (amongst them 2 in PLoS Pathogens, 7 in J. Virology, 2 in J. of Infect Dis).

Assessment of the research team's integration into its environment:

Without doubt, there is a strong socioeconomic and cultural impact that mostly relates to developing countries where vaccination is still poor or not effective. Nevertheless, the recombinant enterovirus strains discovered and yet to be discovered by this team might eventually spread to other countries where vaccination has been discontinued, as already observed for vaccine-derived poliovirus and other emerging viruses. Therefore, knowledge of how and where recombination occurs is of high relevance. The group has obtained financial support from the Gates Foundation to investigate a possible role of immune pressure against non-structural proteins in the selection of recombinants. The team plays a crucial role in the international Pasteur HEV network. Although the group is an Inserm team, it is mainly financed by Pasteur Institute funding. This funding is quite modest.

The group participates in teaching.

Initial funding was very good. Current funding is limited to internal sources (IP and INSERM) and a grant from the Bill and Melinda GATES Foundation. The reason for the cutback in 2011 is not clear.

Assessment of the research team's reputation and drawing power:

The team has international reputation. The international collaboration in the context of poliovirus surveillance is most significant. Possibly, more could be done to attract high level students and post docs from abroad not only for training but rather to bring in new knowledge. In summary, it is a rather small group with 2 senior scientists and a few foreign students.

Assessment of the strategy and 5-year project:

The group wants to continue studying recombinants with respect to the factors that contribute pathological potential with particular emphasis on protein interaction networks. They have already a number of important papers on poliovirus infection and want to extend this work to isolated or laboratory-created recombinants including cell-type specificity of replication, differences in interaction of viral proteins with host proteins etc. All these studies are a logical consequence of the results of previous work and will certainly lead to a better understanding of the interplay of viral and host proteins in neurovirulence.

Conclusion:

- *Overall opinion on the team:*

This is a well-established team of international reputation combining epidemiologic and cell biological aspects of enterovirology.

- *Strengths and opportunities:*

- The team has access to emerging enterovirus variants for study through their international contacts.

- The team studies important mechanisms underlying the emergence of new pathogens

- *Weaknesses and risks:*

- The team receives a weak financial support from Pasteur Institute

- The team has weak external funding

- It is a small team with limited recruitment of post-doctoral fellows

- *Recommendations:*

- The team might seek collaborations with groups having developed novel methodology for the assessment of protein-protein and protein/RNA interactions.

- The team should seek external funding

- It should increase internal collaborations

Team 5: Flavivirus-Host Molecular Interactions

Team leader: Mr Philippe DESPRES

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	/	/	/
N2: EPST or EPIC researchers	/	/	/
N3: Other professors and researchers	2	3	3
N4: Engineers, technicians and administrative staff * on a permanent position	5	4	
N5: Engineers, technicians and administrative staff * on a non-permanent position	/		
N6: Postdoctoral students having spent at least 12 months in the team	3		
N7: Doctoral students	1		
N8: PhD defended	3		
N9: Number of Habilitations to Direct Research (HDR) defended	/		
N10: People habilitated to direct research or similar	2	3	
TOTAL N1 to N7	**11**	**7**	**3**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.
Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-teames-de-recherche/Principes-d-evaluation

• Detailed assessments

Assessment of scientific quality and production:

The research group investigates arboviruses with a special emphasis on the molecular mechanisms of viral replication and host-virus interactions. The team leader is also the head of the National Reference Center for arboviruses that monitors emerging arbovirus infections worldwide. The research into emerging arboviral disease is important and the projects that have been undertaken are in challenging areas. The research is original but not always of high impact in the field.

Over the period of review, the group has had 29 publications in total with the head of the team authoring all but one, a review where the senior researcher is the sole author. Among the publications (collaborative) are 2 PLoS Pathogens, 1 Emerging Infectious Disease, 1 Journal of Infectious Disease and several in Virology and J. Biol Chem. The number and quality of primary publications (n=13) led directly by the research team over the last 5 years is modest relative to the size of the team and the available resources. The 5 most significant papers in the last 5 years are in specialty journals e.g. Virology. The overall publication output are of a type that brings new basic knowledge to understanding virus-host cell interactions, but are not ground-breaking or of immediate translational significance. The number of producers, of staff actively participating in publications is low.

Assessment of the research team's integration into its environment:

The team conducts research on viruses that are endemic in less-developed countries of the world and this is laudable. The group obtained 9 patents over the past 4 years underlining the socioeconomic impact of their research. A comprehensive understanding of arboviruses and production of tools to combat them are worthy goals that have huge socioeconomic impact associated with reduction of the economic burden of disease. The leadership of the national reference center for arboviruses is a valuable public health service, but there is no evidence that this has supported the research agenda. However this responsibility now appears to have been transferred to the French Army.

The team leader was successful in securing external funding with a total of 18 grants including 8 current (beyond 2011) grants. Funding sources include the French ANR as well as the international agencies the Bill Gates Foundation and European framework programs 6 and 7 grants. These external funds provide important external resources in addition to the Pasteur Institute support. Since 2005, the total funding acquired amounts to ~1.5 million Euro, a level that compares favorably with some European countries laboratories.

Assessment of the research team's reputation and drawing power:

No prizes or distinctions have been identified. The team leader is director of the national reference centre for arboviruses and he has been an invited speaker at national and international meetings although no details are given in the report. He is also coordinator of several European research programs.

The group recruited 4 PhD students, 5 post docs and 1 senior researcher during the review period. The personnel have come from laboratories in France and abroad, notably the USA.

The association with the NRC necessitates that the group operates through a wide number of national and European collaborations. The team is clearly collaborative with other academic teams in the Pasteur Institute. It is surprising that there is not greater evidence of collaborations and research output with colleagues in the global network of Pasteur Institute, or with other non-European laboratories.

Assessment of the strategy and 5-year project:

The future work builds on the current research program. The group will continue to investigate the molecular mechanisms of arbovirus pathogenicity. A major new project is focused on investigation of West Nile virus proteins involved in virulence and identification of cellular proteins that they interact with. The group has recently identified human light chain dynein Tctex-1 as a cellular protein that interacts with the ectodomain of the M protein of several flaviviruses at the late stages of infection. The group plans to expand on this finding to examine if the M-TCTex complex associates with the other cellular factors Bax-1, c-Yes and c-Src. Another study is aimed at investigating how Chikungunia virus infects skin keratinocytes, the nature of the innate immune response to this infection and how the pharmacological composition of mosquito saliva affects the host cell. Other projects focus on how flavi- and alphaviruses evade the immune response. In particular how JE viruses can down regulate the interferon response and how Chikungunia and yellow fever viruses can avoid triggering innate immunity by subverting the function of oligo-adenylate synthase proteins. This strategy is low risk and clearly feasible and it is likely to continue to produce an output in basic research, but with a minimal translational impact.

The team plans to continue studying the molecular mechanisms that define the pathogenicity of arboviruses through the understanding of host-cell/virus interactions. The creation of a new entity called "POLARBO" is suggested in the 5-year plan. POLARBO will be "dedicated to arbovirology in terms of expertise, resources and translation of virological research." It is difficult to understand what the main activities of this entity will be and who in practical terms it will interact with since interactions with World Health Organization program such as GOARN are highly unlikely to support an active arbovirus surveillance group. In summary the planned research is relevant to understanding arbovirus infections.

Conclusion:

- *Overall opinion on the team:*

This team has made contributions to the study of arboviral disease and is tackling difficult biological problems. The group has produced publications in basic research and the team head has filed patents that potentially translate the research into diagnostics and vaccine production. The past, current and future research program is solid but not internationally competitive science. The current proposal for the next 4 years is in line with the expertise of the present team.

- *Strengths and opportunities:*

- The team develops a nationally recognized research in the field of emerging viruses.

- The team translates research into new diagnostic tools and vaccines.

- The team runs excellent infrastructures developed to handle Class 3 pathogens.

- The team has national and European collaborations

- The team has a good track record in terms of securing funding and attracting international scientists to the lab.

- *Weaknesses and risks:*

Publications are infrequent and not in high profile/impact journals. Although this does not detract from the quality of the research it lessens the visibility of important research to the wider scientific community. In all, this seems a missed opportunity when there are enviable scientific and translational opportteamies available through the Institut Pasteur network in countries where many of the arboviruses that are the focus of the research are endemic. Since there was little evidence that the NRC provided an important platform for the basic research being undertaken by the team, the transfer of the NRC out of the Pasteur should provide a better opportunity for higher impact research and productivity. At present only very few staff are participating in publications.

- *Recommendations:*

- The team must increase its international standing and visibility via a more innovative research plan.

- The team should develop a strategy for closer interactions with the "Institut Pasteur" network and take advantage of the research opportunities this can provide.

Team 6: Genetics, Papillomavirus and Human Cancer

Team leader: Mr Michel FAVRE

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	1	0	
N2: EPST or EPIC researchers	1	0	
N3: Other professors and researchers	4	0	
N4: Engineers, technicians and administrative staff * on a permanent position	4 (3,5)	0	
N5: Engineers, technicians and administrative staff * on a non-permanent position	2		
N6: Postdoctoral students having spent at least 12 months in the team	2		
N7: Doctoral students	1		
N8: PhD defended	3		
N9: Number of Habilitations to Direct Research (HDR) defended	3		
N10: People habilitated to direct research or similar	5	0	
TOTAL N1 to N7	**15**	**0**	

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-teames-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

The research activities have been centered on the interaction of human papillomavirus (HPV) proteins with host cell factors, in particular proteins implicated in HPV infection and resistance to infection of human keratinocytes. In addition, the team is involved in research and services on several aspects of public health related to the consequences of HPV infections. The scope of the contributions spans basic molecular mechanisms of HPV-host protein interactions, development of new methodology, and public health. The publication record of the team in all these aspects is excellent regarding quality and quantity of papers. The team published 34 primary publications in excellent journals (Nature Methods, J Exp Med, 2 PLoS Pathogens, J Biol Chem, New England Journal of Medicine).

Assessment of the research team's integration into its environment:

The team is composed of 14 members with tasks divided into 3 programs. The adequate integration of the team into its environment is shown by several collaborative projects within the Pasteur Institute in Paris and elsewhere, as well as with other teams outside the Pasteur Institute. Particularly relevant are the activities related to the National Reference Laboratory for papillomaviruses (NRL-HPV) created at the Pasteur Institute in 2008.

The activities of the NRL-HPV serve to help in surveillance as support to the "Institut National de Veille Sanitaire", with agreements with other national institutes, and participation in different research programs on epidemiological aspects of HPV infections.

The socioeconomic and cultural relation is extremely high because of the number of patients infected with human papilloma viruses worldwide. It is of great interest to understand differences between high risk HPVs and low risk HPVs, the outcome of currently implemented vaccination on protection from disease and to unravel the roles of natural mutation and variation (of the virus as well as of the host). It is also important to understand genetic dispositions. All these questions are being very actively pursued in this group. Financing appears adequate. The group not only produced publications on basic research in highly ranked journals but also developed novel methodologies that might be adopted by other groups at the Pasteur Institute. The group is part of a network for genotyping HPVs, which is of high importance for public health.

Assessment of the research team's reputation and drawing power:

The team lists 55 presentations (posters and oral) at international conferences and meetings.

The group participates in several European projects. Members of the group have attended a great number of conferences and actively participated with presentations. Notably, there are not many foreign post-doctoral fellows and PhD students in the team despite the existence of much international collaboration that might foster exchanges of researchers between laboratories. Nevertheless, it did not affect productivity of the group.

Assessment of the strategy and 5-year project:

As the team head is retiring at the end of 2012, no new project was presented. It is however obvious that most of the achievements mentioned above raised new questions that will have to be pursued in the future.

Conclusion:

- *Overall opinion on the team:*

The team is excellent with an excellent scientific output and an original project. The team makes an ideal and successful connection between fundamental research on a high level and medical application and disease monitoring.

- *Strengths and opportunities:*

- The team is efficient in linking fundamental and clinical research

- The identification of the cellular viral protein network is a major achievement

- *Weaknesses and risks:*

None

- *Recommendations:*

The committee supports the continuation of the reference center in another team.

Team 7: Oncogenic Virus Epidemiology and Pathophysiology

Team leader: Mr Antoine GESSAIN

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	1	1	1
N2: EPST or EPIC researchers			
N3: Other professors and researchers	4	4	4
N4: Engineers, technicians and administrative staff * on a permanent position	6	6	
N5: Engineers, technicians and administrative staff * on a non-permanent position	1		
N6: Postdoctoral students having spent at least 12 months in the team	14		
N7: Doctoral students	4		
N8: PhD defended	7		
N9: Number of Habilitations to Direct Research (HDR) defended	2		
N10: People habilitated to direct research or similar	3		
TOTAL N1 to N7	**30**	**11**	**5**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-teames-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

Clinical research and epidemiology project

This group has a well-established position and a world-leading reputation in the discovery, molecular and seroepidemiology of human retroviruses and herpesviruses, and in the relationship between viral epidemiology and ethnogeography. This important activity has been maintained in the current review period, following the discovery by this group and others of a new human retrovirus, HTLV-3, in 2005. The work of the group is published in an appropriate number of moderate-impact (J. Virol) to high-impact (Blood; PLoS Pathogens) journals.

The work on HHV8 has made an identifiable contribution to the molecular epidemiology of the virus and its relationship to ethnogeography. This work has had less general impact than the work on human retroviruses. The productivity of the team is very good.

The team maintains impressive links and collaboration with workers in central Africa (Cameroon) and French Guyana. These are complex and logistically demanding relationships, and the team is applauded for maintaining them. However, there is scope for strengthening these links.

There is good potential to expand the work on genetic determinants of susceptibility to human retroviruses and HHV8. This work is of importance and interest both clinically and scientifically. The proposed work on HTLV-3 epidemiology is of scientific interest, but of limited clinical importance in the absence of evidence of associated disease. These considerations apply with more force to the proposed work on simian foamy virus. The ethnogeography and molecular epidemiology work is of interest, but there is scope for further testing of novel scientific hypotheses.

Physiopathology project

The group has invested a major effort over some years in a study of the effects of HTLV-1 infection on the blood-brain barrier (BBB). This effort is applauded, because it is an attempt to address directly a question of physiological and clinical importance and interest. It is well recognized, however, that there are great technical obstacles to the accurate reproduction of the BBB in vitro, and difficulties in testing resulting hypotheses in vivo. The same considerations apply, although with less force, to the work on the effects of viral infections on the intestinal barrier. These difficulties are reflected in the relatively low number of papers published in the last few years, although some are in good journals.

The recent work of the group on viral myosites has excellent promise. It is still at an early stage of development, but is original and impressive, and merits strong emphasis in the next five years.

Genomic project

The high-density microarray for massively parallel detection of pathogens is a project of admirable ambition. It is important for the team to develop and maintain a clear view of the following points:

1) The competitive scientific position of this project in relation to similar projects elsewhere in the world.

2) The potential to exploit the system either as a resource to other institutions, or commercially.

3) How the system will be maintained in the future, and how it will be kept up-to-date with advances in array technology.

The work in detection and identification of novel lyssaviruses and strains of monkeypox virus is a valuable, albeit small-scale effort, and should be maintained.

Immunology project

It is recognized that the head of the project has only recently joined the team (2010).

The work on HIV proposed in the next 5 years will benefit from the definition of precise aims and testable hypotheses, and from an explicit consideration of the niche that the group proposes to develop in this crowded and highly competitive field.

The proposed work on the human immune response to simian foamy virus (SFV) is of interest scientifically. However, the number of available infected subjects is small, and the clinical importance is limited because of the lack of any associated disease.

Assessment of the research team's integration into its environment:

There is solid evidence of engagement and collaboration with the Pasteur Institute international network. The team participates in teaching and training at the undergraduate and post-graduate level. The team has attracted external funding from France/Europe, but not from outside of Europe. There is no evidence of industry collaborations, but this is offset by the quality of the academic output.

Assessment of the research team's reputation and drawing power:

The head of the team has been recognized through awards and citations for the quality of his academic work. The composition of the team consists mostly of French trained scientists; it is surprising that there is not a track record of training nationals from the Pasteur Institute international network- this would provide important capacity building and stronger collaborative ties that would strategically be in the team's interests. The extent of international collaborations with non-European laboratories appears limited.

Assessment of the strategy and 5-year project:

The Team has developed a rational 5-year plan that represents an extension of their ongoing activities with the addition of new initiatives in immunology and genomics.

There are a number of pathogen detection chips available, both in academic groups and also commercially available. A focus for discussion should be on how the team will differentiate their platform from those that already exist, and how this effort is linked with other Teams in the Pasteur Institute. The following statement found in the team report is perplexing and naïve; "The Pasteur Institute-Bangui is therefore ideally placed to conduct microbiological surveillance programs with identification and molecular characterization of viruses by classical but also broad-spectrum recent molecular techniques such as re-sequencing microarray and high-throughput sequencing." Efforts to identify viral sequences in clinical specimens from OSCCs is a high risk discovery effort. The likelihood of success will depend on the quality of the clinical material and metadata, the capacity to distinguish true signals from the sequence noise and a rational plan for downstream validation experiments.

Conclusion:

- *Overall opinion on the team:*

The team has made a significant international impact during its 12 year history, chiefly in the field of the discovery, molecular and seroepidemiology of human oncoretroviruses. The number and quality of publications is of a high order. The head of the team has a global profile in his field. Members of the group are regularly invited to international meetings. There is strong potential for achievements in several diverse areas in the next 5 years, including genetic determinants of susceptibility to viral infection, viral myositis, high-throughput detection of viruses and identification of novel viruses.

- *Strengths and opportunities:*

The major strengths are the experience and expertise in molecular epidemiology within the team, and certain novel technologies that are under development. These are the qualities that give the team its unique character and identity. The opportunities are to exploit the excellent and long-standing relationship to sites in central Africa and French Guyana and to obtain unique material for study of human genetics and viral epidemiology.

- *Weaknesses and risks:*

The work on molecular epidemiology runs the risk of being seen as descriptive. Work on the effects of viral infections on the blood/brain barrier and the intestinal barrier is high-risk, and should be critically assessed to decide whether the work can produce physiologically relevant, testable results.

- *Recommendations:*

The team is urged to build stronger links with the Pasteur Institute international network, particularly in the field of capacity building and training. The team should also be asked to strategically review if there are opportunities in more translational areas, such as diagnostics, prognostics, clinical or public health intervention studies that are linked in with the academic research focus on retroviruses.

The team should consider carefully the priorities in its planned work for the next 5 years, and put most effort and resources into those areas that have the potential for important scientific novelty. In particular, the genetic determinants of susceptibility to retroviral and HHV8 infection, although demanding, are original and deserving of strong emphasis.

The immunology group needs to define carefully its niche and objectives in the large and intensely competitive field of HIV research. The high-throughput viral detection project should formulate a clear strategy for scientific or commercial exploitation and for its own sustainability as technology advances.

Team 8: Viral NeuroImmunology

Team leader: Ms Monique LAFON

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	0	0	0
N2: EPST or EPIC researchers	0	0	0
N3: Other professors and researchers	3	2	2
N4: Engineers, technicians and administrative staff * on a permanent position	3 (1,5)	3(1,5)	
N5: Engineers, technicians and administrative staff * on a non-permanent position	0		
N6: Postdoctoral students having spent at least 12 months in the team	1		
N7: Doctoral students	1		
N8: PhD defended	2		
N9: Number of Habilitations to Direct Research (HDR) defended	0		
N10: People habilitated to direct research or similar	2	1	
TOTAL N1 to N7	**8 (6,5)**	**5 (3,5)**	**2**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-teames-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

The group was established as a team in 2008 and this is the first intermediate review. The team is relatively small yet is doing cutting edge work in rabies virology. Moreover, the team is moving basic research findings to more practical applications. The team leader has made fundamental discoveries to explain how rabies virus infection promotes neuronal survival and has identified the viral glycoprotein G as the mediator. She has focused on the carboxy terminal tail as the primary interaction center that promotes survival. She has identified specific peptides that may be potential therapeutics. She also has identified mechanisms by which the infected neuron escapes the host innate and adaptive immune response. She has proposed a focused set of new objectives that will move these projects forward with a high probability of success, but also offer opportunities for unexpected discoveries. The committee concluded the team leader is to be congratulated for her vision and focus.

The team lists 14 primary peer reviewed papers, three book chapters, and 5 invention announcements or patents since its establishment. This includes a Science Signaling paper, a Cell paper, and a PLoS Pathogens paper, which will have high impact. The head of the team has given many invited talks and other communications. The publication quantity is very good even for this small group, and the quality and impact is very good to excellent.

Assessment of the research team's integration into its environment:

The transfer of the team from the Neuroscience department to the Virology department a few years ago has proven to be a very good move. The head of the team is a virologist with a neuroscience interest and the team's work is much more appreciated in the Virology department. The team has enjoyed modest funding. The team has received some attractive patents that may lead to clinically useful therapies focused on neuronal survival and blockade of inflammation. The team's interaction with a group working on rabies was not discussed in any detail, but in questions, it was confirmed that the team hosts a student from Africa and the head presented some interesting findings with natural isolates (dog virus and mongoose viruses). Collaborations with neurophysiologists to measure neuron function (electrophysiology) after rabies infection are in place.

Assessment of the research team's reputation and drawing power:

The head of the team is known in the international rabies virus community as evidenced by her invitations to speak at conferences. Most rabies virologists know her by name and by reputation. One of her PhD students won the Hilary Kropowski prize in 2009 offered by the International Society of Neurovirology.

Assessment of the strategy and 5-year project:

The plan is appropriate for this small group. First, the team has these interesting peptides (Neurovitas) that promote neuronal survival when delivered by lentivirus vectors. The team leader believes that Neurovita 1 will work in spinal cord injury and Neurovita 2 will work for epilepsy and chronic pain. The team leader needs to test these ideas. She has proposed a set of five programs with defined objectives (deliveries) to produce and study the neurovita peptides. Her ultimate goal is to transfer these peptides to industrial partners. These objectives are clearly defined and have a high probability of success. While not clearly articulated as a path forward for the next five years, she will focus on a rabies virus modulation of the inflammatory and immune response. This work uses similar methods and technology that identified the G protein tail as the central interface for neuronal survival. The goal here is to find new anti-inflammatory compounds, probably peptide based using lentivirus vectors. The committee experts were less sure of how the team leader was going to do this work with the small staff she has or will have. Her ideas of using MRI small animal imaging and bioluminescence are one way she can optimize the output of her small group.

Conclusion:

- *Overall opinion on the team:*

Original work, novel approaches. Excellent progress overall in this review.

This small group is doing highly focused and relevant work on rabies virus neuropathogenesis. The team leader has made a fundamental discovery identifying the carboxy terminal sequence of the viral glycoprotein G as the mediator of neuronal survival and controlling neuroinflammation. Peptides from this tail segment increase the survival of neurons exposed to various death effectors. The team leader is a dedicated virologist and her small team is well organized. Her plans for the neurovita peptides are well conceived, but her plans for the identification of inflammatory modulating therapeutics based on rabies proteins are not as well developed yet. The idea is very intriguing and worth exploring. The team leader is concerned about the shortage of academic funds to support equipment, lab expenses, new postdoc – she will have to get external grants to do this. Her two years of Carnot Institute funding are almost up. Reduction of a technician will slow her work down.

- *Strengths and opportunities:*

Fundamental discovery of the role of the G protein cytoplasmic tail in neuron survival and inflammation opens new avenues for basic biology and translational research.

- *Weaknesses and risks:*

Funding is an issue; funding for transfer of work to an industrial partner is not secure. Reduction of a technician will slow her work down.

- *Recommendations:*

The team leader should make every effort to get this work funded.

Team: 9 Hepacivirus and Innate Immunity

Team leader: Ms Eliane MEURS

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors			
N2: EPST or EPIC researchers	1	2	2
N3: Other professors and researchers	2	2	2
N4: Engineers, technicians and administrative staff * on a permanent position	6(3,15)	6 (3,15)	
N5: Engineers, technicians and administrative staff * on a non-permanent position			
N6: Postdoctoral students having spent at least 12 months in the team	1		
N7: Doctoral students	4		
N8: PhD defended	5		
N9: Number of Habilitations to Direct Research (HDR) defended			
N10: People habilitated to direct research or similar	2	2	
TOTAL N1 to N7	**14 (11,15)**	**10 (7,15)**	**4**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-teames-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

The hepacivirus and innate immunity group comprises three groups focusing on hepatitis C virus (HCV) evasion of innate immune signaling; the role of HCV and lipid biosynthesis pathways in the viral lifecycle and the role of Hepatitis B virus (HBV) encoded HBx protein in carcinogenesis, respectively. The scientific achievements of each group are summarized below:

HCV evasion: The major focus is to understand the mechanisms underlying HCV evasion of host interferon (IFN) responses with the goal of uncovering new therapeutic approaches to boost immune control of this virus. In collaboration with a group at McGill University, Montreal, CA, the team leader reported a mechanism for IKKe association with MAVs that promotes NF-kB activation and expression of various pro-inflammatory mediators (Mol Cell 2009). This productive collaboration identified a novel negative regulatory role for mitotic Polo-like kinase to control MAVS/TRAF3 interactions (JBC 2009) and more recently identified the interactive site between the two proteins (Cell Res 2011), providing potential therapeutic targets. It's been known for some time that HCV induces a number of interferon stimulated genes (ISG) in vivo, with limited evidence for interferon expression. The team recently reported an explanation for this observation showing that HCV recruits PKR early in infection, ahead of RIG-I, to re-target the MAVS signaling pathway to induce a number of ISGs, including ISG15, that are pro-viral and limit IFN expression (PLos Pathogens, 2011). This work unravels a new signaling pathway triggered by HCV which suggests that the use of PKR inhibitors might be relevant in the treatment of some HCV patients.

HCV and lipoproteins: Several reports in the literature documented the association of HCV RNA with host lipoproteins VLDL and LDL in the plasma from infected subjects. For this project, investigators designed in vitro studies to investigate the biological significance of host lipoproteins in the HCV lifecycle, demonstrating a role for lipoprotein lipase in bridging HCV association with cell surface GAGs (Cell Micro 2007) and demonstrating that exogenous lipoprotein lipase could inhibit HCV entry (PLos One 2011). HCV-lipoviral particles are actively being studied in terms of their composition and biology in a number of labs in Lyon, Heidelberg, Newcastle and Kentucky, the major road-block is the difficulty in propagating primary virus strains in vitro which limits the biological studies that can be conducted with plasma derived lipoprotein-associated low density particles. An independent line of investigation studied virus encoded core transport between the nucleus-cytoplasm (PLoS One 2011) and the role of the microtubular network in core trafficking in HCV assembly in collaboration at group at MRC, Glasgow (Traffic 2008; JBC 2009). Finally the authors have been studying in collaboration with several investigators in the International Pasteur Network the alternative reading frame protein (ARFP, core +1) and its potential for early serodiagnosis (J Clin Virol 2010; Plos One 2011).

HBV: One researcher joined the Hepacivirus group in 2010 following the closure of another team. Thus, her work focuses on HBV and in particular on the role of virus encoded HBx in hepatocarcinogenesis, demonstrating that HBx interacts with CREB co-activators CBP/p300 and this in turn may regulate cellular proliferation (JBC 2007), more recently her laboratory demonstrated that HBx increases HBV transcription/replication illustrating a previously unknown mechanism of HBV transcriptional activation where HBx interferes with the inactivation of CREB by the PP1 and HDAC1 complex (Science Signalling, 2012). HBx is undoubtedly a fashionable protein to study with over 90 PubMed citations in 2011-2012, with the majority of studies focusing on HBx biology in immortalized cell lines. If there is an opportunity for this researcher to translate her recent observations into clinical material this would seem like the optimal strategy to increase the impact of her work.

Over the 2007-2011 period the group published a total of 29 primary research papers (11 as communicating author) and 4 review articles in journals with middling impact factors ranging.

Assessment of the research team's integration into its environment:

The groups list a range of national and international collaborators associated with each of the projects, many of these collaborations have resulted in publications. However, there appears to be more limited collaborations with "Institut Pasteur" colleagues. For example, no current or future collaborations are listed with the Hepatitis B Pathogenesis group.

The committee had limited evidence to judge the mentoring of early-career scientists.

Current funding from ANRS, ACIP and INCA amounts to approx, 290,000 € which is modest for three PIs. No EU Framework consortia memberships are listed.

Assessment of the research team's reputation and drawing power:

The group lists an extensive number of external seminars and meeting presentations (n=76) as evidence of the team's reputation, where both PI and junior members of staff present their work at national and international meetings. The team leader has been on the organizing committee for three meetings since 2006-to present time, the other two team members have helped to organize one meeting each in this time period. The team leader is editor for PloS One.

The recruitment of one staff scientist is certainly very promising and reflects a certain attractivity of the host laboratory.

Assessment of the strategy and 5-year project:

HCV evasion (1) Viral signals recruiting PKR/MAVS pathways. To identify steps in the HCV life cycle that recruit PKR, preliminary data suggest an endocytic step is required. The authors intention to study HCV receptor signaling is not well justified or explained as to how such experiments would be performed or interpreted given the complex multi-step receptor-dependent entry of HCV. Additional experiments to assess the role of core protein, replicating RNA are poorly explained.

(2) To study the role of peroxisomes and mitochondria on PKR/MAVS pathway. The authors propose to study the localization of MAVS protein and mCherry-PKR trafficking in HCV permissive hepatoma cell lines. Lentiviral vectors will enable the establishment of cell lines constitutively expressing these proteins. In addition, they propose to investigate the effects of HCV-receptor engagement, proposing to use HIV GAG-GFP pseudoparticles expressing HCV E1E2 glycoproteins for live cell imaging. Parallel experiments will examine the effect of compounds known to affect peroxisome or mitochondrial function on PKR trafficking and HCV replication. The authors propose to expand these studies to other hepatotropic viruses (HBV, Dengue, YFV). Involvement of organelles and in particular of peroxisomes in signal transduction is certainly a timely topic, however, minimal information is provided to allow in depth assessment of the project.

(3) To identify partners of PKR/MAVS pathway. To study the importance of TRAF and STING proteins through various biochemical approaches and in parallel to use mass spectrometric analysis in collaboration with NIID in Japan to identify partners.

(4) To identify PKR inhibitors to control virus infection. This is a long range project aiming to isolate peptides, in collaboration with a group in Pamplona, Spain, that antagonize PKR with the goal of promoting IFN expression and innate control of virus infection. The authors propose to screen a phage 15-mer peptide library. It is not clear what they will screen against. Since PKR crystal structure is known –perhaps project might be expanded to include a rational design approach.

HCV and lipoproteins (1) Role of ATP-binding Cassette transporter A1 (ABCA1) in HCV infection. Studies will address the effect of silencing or overexpressing ABCA1 on HCV infection.

(2) The role of core-microtubule interactions in HCV infection. Biochemical characterization of core-microtubulin interactions. It is not clear how the authors will study microtubule stability and whether this will be performed in living cells?

(3) Biomarkers for early diagnosis of HCV associated HCC in Africa, SE Asia and EU. New treatments and early diagnosis of HCC are urgently needed, however, the minimal information provided does not allow external review from already published studies. There is no clear experimental plan, information on clinical status, power calculations or analytical methodologies provided.

HBV (1) Role of PML nuclear bodies in HBV infection. A recent publication reported a role for PML NB in HBV replication, concluding that they cooperate with HBV-core and HDAC1 on the HBV covalently closed circular DNA basal core promoter to form a positive feedback to reduce HBV during chemotherapy and radiotherapy. Some of the experiments proposed by the team are included in this publication that the lab may now need to reconsider.

(2) Identify interacting partners of HBx and DDB1 E3 ubiquitin ligase. Current biochemical approaches have identified HBx/DDB1 binding proteins in HepG2 using FLAG-HA tagged proteins. Future experiments will validate these proteins for their role in HBV replication by conventional siRNA and over-expression approaches. Selected proteins will be studied for their effects on HepG2 tumorigenic potential and expression in tumor and non-tumor liver tissue from HBV infected subjects.

(3) Structural characterization of HBx/DDB1 E3 and candidate proteins. These experiments will be conducted with the structural virology team and are novel, high risk but high gain!

Conclusion:

- *Overall opinion on the team:*

There is international recognition for HCV/HBV and PKR work. Most publications are however, in mainly middle-ranking journals over the 2007-2012 review period. The project on peroxisome involvement in signaling is timely, although not well defined. The project on HBx is interesting and represents a logical follow-up of recent findings. It is not clear however how much these two projects are interconnected.

- *Strengths and opportunities:*

The recent recruitment a staff scientist (outstanding track record with recent primary publications in Nature Cell Biology, PNAS...) is an asset and strengthens the 5-years perspectives. In the HBx-DDB1 project, the proposed collaborations with the team working on carcinogenesis and with the team of structural biology are expected to increase competitiveness.

- *Weaknesses and risks:*

The majority of proposed studies are an extension of existing work – specific caveats are listed under each project above.

There is limited evidence to translate in vitro observations to the in vivo setting. This is particularly important as we enter a new era of anti-viral drug testing in HCV where it will be vital to understand why patients relapse from drug treatment(s).

This team functions as an aggregate of 3 independent research laboratories with minimal connections between projects rather than as a joint venture. This is indicative of the current status of hepatitis virus research at the Institute.

- *Recommendations:*

Hepatitis virus research at the Pasteur Institute should be reorganized as recommended in the general recommendation section for the whole department.

Team 10: Pathogenesis of hepatitis B virus

Team leader: Ms Marie-Louise MICHEL

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	0		
N2: EPST or EPIC researchers	1	1	1
N3: Other professors and researchers	4	1	1
N4: Engineers, technicians and administrative staff * on a permanent position	3 (2,25)	3(2,25)	1
N5: Engineers, technicians and administrative staff * on a non-permanent position	1		
N6: Postdoctoral students having spent at least 12 months in the team	3		
N7: Doctoral students	1		
N8: PhD defended	2		
N9: Number of Habilitations to Direct Research (HDR) defended			
N10: People habilitated to direct research or similar	2	2	
TOTAL N1 to N7	**13 (12,25)**	**5(4,25)**	**2**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-teames-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

The team was created in 2007 at the time of retirement of the previous head. A scientist joined the group in 2010. The team leader and her colleagues have made extensive contributions to our knowledge of HBV pathogenesis, particularly the role of HBV PreS proteins and immunity using a transgenic mouse system. The group focuses on HBV immunopathogenesis and the vaccine therapy of chronic HBV carriers. The group has made fundamental discoveries, some of which may translate to better diagnostics and therapies for treating human chronic HBV infection. The laboratory identified the non-structural proteins HBx and HBSP as targets of the host immune response. In parallel they demonstrated that a DNA vaccine could activate the immune response in chronically infected patients. They have constructed a recombinant HBV genome that expresses a core gene with a non-viral T cell epitope and showed that this virus triggers T cell responses in mouse models of HBV infection. With the Pasteur Institute in Shanghai, using systems biology methods, they have identified characteristic signatures in hepatocellular carcinomas (HCC) that may help in the predicting clinical outcome of HBV-related liver cancer. They also have found that fine-tuning of a beta catenin interacting protein (FHL2) is critical for carcinogenesis associated with activation of the Wnt signaling pathway. Specific comments are listed below:

The productivity is average for a small group. The publication record for the past few years is modest both in the number (10 peer reviewed publications deriving from direct work of the team).

Assessment of the research team's integration into its environment:

The team leader has integrated her studies with clinical groups in Paris and in Europe. The group has trained several PhD students and postdoctoral fellows. The team leader and the staff scientist both lecture in various courses at the Pasteur Institute. However, it is not clear to the experts of the committee how interactive the group is with colleagues at Institut Pasteur, the lack of communication with the other team working on HBV is noteworthy.

Assessment of the research team's reputation and drawing power:

It is difficult for the committee to judge based on the material provided. The executive summary only lists five invited lectures over 2007-2011 period for the team leader and no mention is found about editorial board membership, grant committee participation etc.

Assessment of the strategy and 5-year project:

The plan continues to build on previous work in close collaboration with clinical institutions. The first aim is to identify host immune responses to HBV with the goal of designing novel therapies. The AAV vector carrying the HBV genome delivers infectious HBV into mice. This model is a surrogate for human infection and for testing new therapeutic vaccine candidates. There are considerable problems in extending DNA immunization studies from mice to humans, no matter how representative the mouse system is through use of the appropriate transgenes. No contingency plan is provided if the clinical trial proves disappointing in phase II. The second aim is to study viral –host interactions in HCC. They will first use Mdr2-/- mice, which develop cholestatic hepatitis and hepatocellular carcinoma, and the AAV/HBV vector to look at the contribution of HBV in a chronic inflammation background. Whilst there is always value in studying CTL and humoral responses in chronically infected patients using well-defined cohorts, there is little new in what is proposed. Next they will participate in a European consortium to do a genome-wide analysis of transcription, epigenetics, and high order chromatin alterations that occur in liver cancer in the mouse and human. They also will attempt to identify oncogene pathways activated in liver cancer to improve diagnostics and therapeutics. The plan is ambitious and it is not clear how much can be done before the team leader's retirement. Plans for the group and whether the staff scientist will take over the projects are not mentioned.

Conclusion:

- *Overall opinion on the team:*

The group is at a transition point with the retirement of its head in three years and contingency plans were not provided. Nevertheless, the future plans will continue to build on the path defined by previous studies and collaborations. The probability that the group will continue to do solid research is high.

- *Strengths and opportunities:*

The group is well focused on HBV pathogenesis and has done important work with diagnostic and therapeutic potential.

- *Weaknesses and risks:*

The value of the mouse models for human hepatitis and cancer remains to be seen. However, one questions just how far this work can be taken in terms of making valid comparisons with human disease, when there is abundant clinical material and other arguably more relevant models of hepadnavirus pathogenesis available.

The probability of success in finding new diagnostics and therapeutics is much less certain.

- *Recommendations:*

At the very least, the team needs to present a more cogent case for the work they plan to do in the context of work being carried out elsewhere.

Team 11: Structural Virology

Team leader: Mr Félix REY

Workforce

Workforce	Number on 06/30/2011	Number on 01/01/2013	2013-2017 Number of producers**
N1: Professors or assistant professors	1	1	1
N2: EPST or EPIC researchers	2	2	2
N3: Other professors and researchers	9	5	4
N4: Engineers, technicians and administrative staff * on a permanent position	4 (3.4)	4 (3.4)	
N5: Engineers, technicians and administrative staff * on a non-permanent position	1		
N6: Postdoctoral students having spent at least 12 months in the team	10		
N7: Doctoral students	3		
N8: PhD defended	3		
N9: Number of Habilitations to Direct Research (HDR) defended	1		
N10: People habilitated to direct research or similar	4	2	
TOTAL N1 to N7	**30 (29,4)**	**12 (11,4)**	**7**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-teames-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

The group's scientific program can be defined by three main axes: capsid assembly, viral replication and viral envelope glycoproteins. Their work on the RSV nucleoprotein structure in complex with RNA had a major impact on the field and provided a structural basis to understand RSV replication. The group also continued their successful work on envelope glycoprotein structures and extended it to the cellular fusion protein Eff1 that shows surprising structural homology to class II fusion proteins. The overall work of the group is of high relevance and originality. The structure-based approach employing innovative integrated methods allows elucidating novel relationships between proteins and viruses that are not evident from sequence analyses.

The group is one of the world leaders in structural virology with a world-renowned flagship program determining the structures of the envelope proteins of a variety of viruses that has had the highest impact in the past. They continued this successful path and the high impact of the group is highlighted by its total of 67 publications with the head of the team authoring 33. Among the top publications are 1 Nature, 2 Science, 3 PNAS, 3 PLoS Pathogens, 1 Cell Host Microbe, 2 EMBO and 2 Structure papers. This is an outstanding output both in quality and quantity and the constant high quality of publications is extraordinary. Notably the progress report lists 7 structures, which have not been published yet!

All staff contributed to the success of the group and participated adequately in the publications. The general scientific output of the group is further underlined by the high number of publications of staff members that do not include the head of the team indicating a prosperous balance for scientific freedom.

Assessment of the research team's integration into its environment:

The group obtained 4 patents over the past 4 years underlining the socioeconomic impact of their research.

A comprehensive understanding of viral entry is highly sought after and the team's research is directly aimed at achieving this goal. The contribution to medicine and vaccines through research into viral envelopes entry has huge socioeconomic impact associated with reduction of the economic burden of disease.

The team was very successful to secure external funding with a total of 24 grants including 6 current (beyond 2011) grants. Funding sources include important French organizations such as ANR, ANRS, FRM and Sidaction as well as international agencies including the Bill and Melinda GATES Foundation and European framework program 6 and 7 grants. These external funds provided important external resources in addition to the Pasteur Institute support and underline the international reputation and the scientific output of the team.

Assessment of the research team's reputation and drawing power:

The team leader was elected member of the Acadaemia Europaea, he received the René and Andrée Duquesne Price, became a member of European Academy of Microbiology and was elected to the French Academy of Sciences. Together, the number of distinctions received during the past period, underscore the scientific excellence of the team leader and his group. The team leader is also a member of scientific advisory boards of Pasteur institutes in China, Korea and Uruguay and an invited speaker at numerous national and international conferences including Gordon research conferences etc, further underlining his standing in the scientific community. It was noted that no participation of staff members in meetings and conferences was listed.

The group recruited 3 PhD students and 8 post docs during the last period mostly from labs abroad (USA, Germany). Two of the post docs have since then obtained permanent (chargé de recherche) Pasteur positions.

The team collaborates with numerous foreign laboratories and particpated in international programs such as the Bill and Melinda GATES foundation PDVI, european framework 6 and 7 programs and a FP7 Marie curie ITN network.

Assessment of the strategy and 5-year project:

The future work builds on the success of the current research program. The group will finish the structure function analyses of 7 structures already available for publication. They will continue their program on virus assembly employing FIV Gag as a model system. They will further engage on the challenging objective to obtain high-resolution structural information on the RNA-dependent RNA polymerase from single stranded negative strand RNA viruses such as RSV, a project that is highly complementary to their previous work on the RSV N and P proteins.

Work on viral polymerases is also to be extended to the heterotrimeric influenza virus polymerase, which can be produced in yeast cells. Methods for protein production for both challenging projects are already in place. The group will further continue their successful program on viral envelope glycoproteins with a special focus on predicted class II viral fusion proteins such HCV E2 and related viral glycoproteins and Hantavirus Gc. Although these projects are high risk and challenging, the group has assembled an impressive arsenal of tools that will help to obtain high resolution diffracting crystals. Lastly, they will also continue their work on herpes virus glycoproteins (Pseudorabies virus, CMV gH/gL, Varicella-Zoster virus gE/gI) in order to understand their fusogenic potential. Further structural work is also planned on viral glycoproteins (gH from herpes and CMV, hantavirus Gn and West Nile virus E) in complex with integrin αvβ3 heterodimeric receptors. In summary the planned research is both original and highly relevant to understand viral replication and fusion machinery. The group takes considerable risks in trying to tackle very challenging projects; however, its track record has proven they have the capacity to succeed. Furthermore, all projects are carried out in the context of collaborating labs, which will provide important functional insight into the projects. In addition, the integration of functional research on flaviviruses has great potential for future detailed structure-function analyses.

Conclusion:

- *Overall opinion on the team:*

This team has made outstanding contributions to structural virology, and enjoys high visibility in the field. The group is highly productive, and is the leading group in structural virology in Europe. They tackle difficult exciting biological problems where the production of proteins is often the most challenging part of the project. The past, current and future research program is solid and exciting science. The current proposal for the next 5 years is feasible and in line with the expertise of the team.

- *Strengths and opportunities:*

- The group has a strong and foresighted leadership.

- It holds an outstanding international reputation.

- The PI is an international leader in the field of virus entry machines.

- The team developed excellent infrastructures to tackle the structural projects.

- The team has a track record to make complicated projects work.

- The team may outreach to important collaborations where necessary.

- The team has a proven track record of success in terms of securing funding, attracting international scientists to the lab and producing high quality research papers.

- The accumulated unpublished structural work promises already further high profile publications

- *Weaknesses and threats*

- No major weakness has been identified.

- *Recommendations*

- Keep up the outstanding track record

Team 12: Viruses and RNA interference (VIA)

Team leader: Ms Maria Carla SALEH

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors			
N2: EPST or EPIC researchers			
N3: Other professors and researchers	1	1	1
N4: Engineers, technicians and administrative staff * on a permanent position	3 (1,75)	0	
N5: Engineers, technicians and administrative staff * on a non-permanent position	1		
N6: Postdoctoral students having spent at least 12 months in the team	2		
N7: Doctoral students	1		
N8: PhD defended	0		
N9: Number of Habilitations to Direct Research (HDR) defended	1		
N10: People habilitated to direct research or similar	1	1	
TOTAL N1 to N7	**8 (6,75)**	**1**	**1**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-teames-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

This is a young team that has established a high quality and original research program, to study the innate immunity in insects mediated by small RNAs in Drosophila and mosquitoes. The team has already produced some excellent publications, including seminal discoveries on the systemic spread of RNAi in Drosophila and that RNAi is the major antiviral response against negative strand RNA viruses in insects (papers in Nature and PNAS). In addition to those noted in the report a new publication in PloS One on ping-pong-dependent piwiRNAs in arbovirus-infected mosquito cells is particularly meritorious. Although the number of papers published by the team is relatively low, their quality is exceptional.

Assessment of the research team's integration into its environment:

The team leader is an extremely dynamic individual who has quickly built up a well-funded team, including winning a substantial ERC grant.

Assessment of the research team's reputation and drawing power:

The team leader has been an invited speaker at several prestigious conferences. The team has an impressive international composition and has attracted one short-term EMBO fellow.

Assessment of the strategy and 5-year project:

This is an exciting program at the cutting edge of this relatively new area of research. The proposed research will lead to important discoveries concerning the innate immune responses of insects in both Drosophila and the more applied mosquito models that will have high impact in the field.

Conclusion:

- *Overall opinion on the team:*

This is an excellent team with an exciting research program. The Pasteur Institute has made an excellent appointment.

- *Strengths and opportunities:*

- The research area is highly topical and one that will expand in the coming years.

- The team is well placed to be at the forefront of the international effort.

- *Weaknesses and risks:*

The committee noted that the team must have appropriate access to BSL3 facilities to pursue some aspects of the proposal that concern arboviruses of clinical significance.

- *Recommendations:*

Access to BSL3 lab space is required.

Team 13: Virus and Immunity

Team leader: Mr Olivier SCHWARTZ

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors			
N2: EPST or EPIC researchers			
N3: Other professors and researchers	7	6	6
N4: Engineers, technicians and administrative staff * on a permanent position	2 (1,80)	2 (1,80)	
N5: Engineers, technicians and administrative staff * on a non-permanent position			
N6: Postdoctoral students having spent at least 12 months in the team	4		
N7: Doctoral students	3		
N8: PhD defended	4		
N9: Number of Habilitations to Direct Research (HDR) defended			
N10: People habilitated to direct research or similar	1	1	
TOTAL N1 to N7	**16 (15,80)**	**8 (7,80)**	**6**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-teames-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

The group studies the molecular mechanism of direct lymphocyte-to-lymphocyte HIV-1 spread via so-called virological synapses, structures that appear to resemble immunological synapses. The team has made very important contributions towards the understanding of this process, notably the role of ZAP-70 in synapse formation and the role of interferon in replication. Their further studies elucidated the role of the restriction factor tetherin in cell-to-cell transfer and contributed to the discovery of the dendritic- and myeloid-cell specific restriction factor SAMHD1. The second axis concerns HIV-1 and immune activation. The group identified a novel function of ABOBEC3 and described the role of TLR7 in sensing HIV-1 in pDCs. In contrast to HIV-1, non-pathogenic foamy viruses trigger a substantial type-I interferon response in human cells. The third axis is on Chikungunya virus and the cellular immune response upon infection. The relevance, originality and impact of the research are excellent, as indicated by high quality publications in journals with high impact factors.

The group published 35 publications during the last period. The quality of publications is impressive and includes 11 principal publications (1 Nature, 2 Immunity, 1 Nature Immunology, 3 J. Exp. Med., 1 Cell Host Microbe, 4 PLoS Pathogens and 1 EMBO J.: among them 4 as first and last author). The overall high quality of publications is excellent and puts the group at the forefront of research in its domain. Permanent staff made important contributions to the publications.

Assessment of the research team's integration into its environment:

No patent applications are listed. The team leader is very active in the dissemination of science with the general public as highlighted by the numerous interviews for newspapers, radio and TV stations.

The group is very well integrated into the Pasteur Institute environment. Numerous collaborations within the institute exist and resulted in common publications.

The group was very successful in securing funding. They obtained 18 grants, out of which 6 are ongoing. Two new grant applications are pending. The group is part of a LABEX initiative, which provides long term funding. Funding sources are mostly the ANR, ANRS and Sidaction, as well as 2 European grants. The amount of external funding largely extends institutional funding. The group also participates in activities of the ANRS HIV vaccine network and is part of the new Vaccine Research Institute, funded by a LABEX grant.

Assessment of the research team's reputation and drawing power:

The national and international recognition of the PI is highlighted by two recent awards, the FRM Prix Louis Tartois and the Prix Pasteur Valery-Radot. Furthermore, the team leader was elected an EMBO member in 2008 in recognition of his excellent international standing and research contribution.

The team lists more than 40 invitations to international conferences and institutional seminars. Most notably, he was an invited speaker at 3 Keystone Conferences, the EMBO meeting, a European Congress of Virology, International AIDS Society and AIDS Vaccine meetings underscoring the group's international visibility.

The composition of the group is international. The permanent staff (former post doc) obtained her PhD in Italy and current post docs include recruitments from Spain and Germany.

The group participates successfully in national (LABEX etc) and international programs (EU FPs) and has a number of successful collaborations with foreign labs (Heidelberg; Genève; Oxford; Pasteur Institute Hong Kong; Illinois; UCSF; Pasteur Institute Korea).

Assessment of the strategy and 5-year project:

The long term project of the group builds on the current successful research activities. The group will continue to study the formation and function of virological synapses for HIV-1 transmission, which is of high relevance to understand HIV-1 pathology. One key objective is to elucidate the role of kinases in HIV-1 cell-to-cell transfer by employing kinase inhibitors and siRNA screening targeting 710 human kinases. It is highly likely these assays will come up with 'hits' and open up new research opportunities. In addition, new cell culture systems, such as co-cultures of T-cells and DCs, will be established to study the net effect of Nef on virus replication.

HIV and T-cell motility – Nef seems to affect localization and mobility of infected cells (Nef effect on filopodium-like structures). Nef will be tested in its natural environment. The overall goal of this project is ambitious but provides a novel important approach to understanding the role of Nef in pathogenesis.

The second axis of the lab concerns HIV and immune activation. The main objective is to elucidate how HIV-1 triggers an innate immune response in hematopoietic and non-hematopoietic cells. The group has previously developed a co-culture system (pDCs, PBMCs and HIV-1 infected donor cells) to study interferon responses depending on the type of donor cell. The role of SAMHD1 will be analyzed in monocyte-derived DCs and pDCs.

This setup will allow a better characterization of the early steps of the immune responses against HIV-1.

The team develops also a project on the impact of HIV candidate vaccine on DC function and T-cell activation. Within the ANR's HIV vaccine network they will analyze vaccine candidates with respect to their effect on T cell activation and viral spread. This work will be highly relevant to understanding the influence of HIV on DC function, cytokine secretion and antigen presentation to T cells.

Third axis is on the role of proteins involved in Chikungunya infection. Among a set of ~ 100 cellular proteins identified as required for infection, a subset of these will be performed with a view to identifying proteins involved in virus cell interaction, entry and fusion.

The projects are feasible and should provide novel exciting insight into the function of virological synapses, interferon signaling and virus infection, as well as Chikugunya host interaction.

Most of the current funding expires in 2012, except LABEX. Two major grant applications are pending and will help to secure extramural funds.

The research into the virological synapse, and the regulation of innate immune responses to HIV infection, is important and original. Although there is significant competition, the group has consistently made original insights and contributions to knowledge in this area. The choice of projects comes with certain risk taking, which is however manageable given the expertise and track record of the group.

Conclusion:

- *Overall opinion on the team:*

- The PI Selects important research topics.

- The team has an excellent publication record and excellent international visibility.

- *Strengths and opportunities:*

- The group has established important cellular systems that put them at the forefront of their competitive research area.

- The team leader has an excellent leadership.

- *Weaknesses and risks:*

The Chikungunya project is interesting but might deviate important limited resources from the main topic HIV. However, this virus is spreading in Europe and could become a significant health risk.

- *Recommendations:*

Continue the excellent work.

Team 14

Viral Genomic and Vaccination

Team leader:

Mr Frédéric TANGY

Workforce

Workforce	Number on 06/30/2011	Number on 01/01/2013	2013-2017 Number of producers**
N1: Professors or assistant professors	-	-	-
N2: EPST or EPIC researchers	3	3	3
N3: Other professors and researchers	1	2	2
N4: Engineers, technicians and administrative staff * on a permanent position	5 (4.3)	6 (5.3)	
N5: Engineers, technicians and administrative staff * on a non-permanent position	1		
N6: Postdoctoral students having spent at least 12 months in the team	4		
N7: Doctoral students	3		
N8: PhD defended	6		
N9: Number of Habilitations to Direct Research (HDR) defended	1		
N10: People habilitated to direct research or similar	3	4	
TOTAL N1 to N7	**17(16.3)**	**11(10.3)**	**5**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-teames-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

The team is organized in 5 small research groups, each headed by a permanent scientist, and including postdoctoral fellows, PhD students and technicians. The team recently added 2 permanent scientists. Between 2007 and 2011 a major focus of the team has been translational research related to the development of measles virus as a live vaccine vector. Additionally, the group also investigated virus-host cell molecular interactions, with a focus in measles and Chikungunya. The number of publications (n=44) over the 5-yr review period is modest relative to the size of the group and its setting in the Institute Pasteur. Less than half the publication output is led by members of the team. The most high profile publication is in PLoS Pathogens in 2009 relating to cellular targets of the virulence protein C of human parainfluenza virus type 3. The remaining publications where members of the team are in leading authorship positions are in lower profile specialty journals.

Assessment of the research team's integration into its environment:

The team has generated 8 international patents and 3 industrial R&D contracts with pharmaceutical and biotechnology companies, in Belgium and Austria. The advancement of a recombinant measles-HIV vaccine candidate into early phase clinical trials is a very notable achievement.This very high capacity to develop translational research projects is certainly one of the strengths of the team and partially offsets the modest publication track record.The team leader and another permanent scientist have also demonstrated an ability to obtain external funding from national and European funding agencies, and from R&D collaboration contracts with industrial partners.

Assessment of the research team's reputation and drawing power:

There is no evidence provided of prizes/distinctions received by the team members in the review period. Members of the team have participated in national and international meetings. From the CV's provided, it appears that most members of the team have received their scientific training in France. It is important to note that 6 PhD theses were defended since 2007. There is good evidence of academic, and to a greater extent, industrial collaborations within France and elsewhere in Europe. Finally, the team leader and some other scientists of the team are actively involved in teaching activities, both in Pasteur Institute and French universities

Assessment of the strategy and 5-year project:

Much of the focus in the 5-year plan is around refinement of the Measles Vaccine-based vaccine vector approach, with specific efforts in development and testing of MV-based vaccines against HIV, malaria, dengue, influenza, RSV and Chikungunya. This very broad portfolio of planned vaccine targets comes with the risk that the team does not have the necessary expertise to be able to competently test immunogenicity and efficacy in a variety of different animal models. Furthermore, given the prominence of the MV theme in the 5-year plan it is disappointing that the early stage clinical trial of the candidate MV-HIV vaccine (began 2010) cannot be more extensively reported on over 2 years later. Despite these reservations, the work is sufficiently novel and with potentially high impact on very important diseases that it should be encouraged and supported. This support should be balanced with the understanding that the promising pre-clinical results will, in all probability, not be directly translated to human volunteers. This is not a criticism of the science, just a statement of the reality of moving vaccine candidates from animal models to humans. In the scenario where results from human volunteer studies are less than compelling, it will be important to know when to stop deploying research resources to this vaccine methodology.

A second element of the 5-year plan focuses on drug-mediated enhancement of innate immunity as a broad-based anti-viral strategy. This strategy has scientific merit for its potential to discover new pathways/functions in innate immunity. The team has interesting preliminary data but further work will be required to identify mechanisms of action.

The team proposed to develop several sub-projects relating to – a) the potential role of biased nucleotide composition for live viral vaccines, b) the potential role of RNA sensing receptors, c) characterization of the mechanisms of attenuation of measles virus, d) characterization of a new cellular receptor for the measles virus and e) mapping of hundreds of virus-host protein interactions for multiple viral systems. These were generally not tight, hypothesis-driven proposals and represent a worrying sign of over ambition and lack of focus in the research program.

Conclusion:

- *Overall opinion on the team:*

The team has a track record of publications that is quite modest in volume and quality for a group of its size and resources. Nevertheless, it has made very significant translational achievements in pushing through a candidate HIV vaccine to early phase clinical trials. The team should be supported in their efforts to further develop the MV approach but this should also be coupled with a commitment to more and higher quality publications in the very near future. There should also be a rational approach to determining the amount of resources committed to the MV approach with pre-defined "go/no-go" decision points around the viability of the different vaccine projects.

- *Strengths and opportunities:*

The team made significant translational research achievements.

- *Weaknesses and risks:*

The number of proposed "discovery" projects is concerning given the absence of a hypothesis in many of these projects and the recent modest publication track record of the team. The team should be encouraged to triage these projects and focus only on the highest quality/impact opportunity.

- *Recommendations:*

There is little evidence of immunological expertise in the track record of the team and therefore it should consider collaborations that bring in this expertise to maximize the research opportunities afforded by vaccine trials in non-human primates and human volunteers. This immunological expertise will be important in refining the MV approach.

Team 15: Biology of Emerging viral infections

Team leader: Mr Sylvain BAIZE

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	0	0	0
N2: EPST or EPIC researchers	0	0	0
N3: Other professors and researchers	2	3	1
N4: Engineers, technicians and administrative staff * on a permanent position	4 (3.8)	4	
N5: Engineers, technicians and administrative staff * on a non-permanent position	1		
N6: Postdoctoral students having spent at least 12 months in the team	0		
N7: Doctoral students	1		
N8: PhD defended	1		
N9: Number of Habilitations to Direct Research (HDR) defended	0		
N10: People habilitated to direct research or similar	1	2	
TOTAL N1 to N7	**8 (7,8)**	**7**	**1**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-teames-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

Important work has been performed, mostly to decipher the bases of Lassa virus virulence. This ranges from obtaining a reverse genetic system for this virus to the comparison of immune responses to the virus in diseased and less affected animals.

This group analyzed the different components of the immune response against these viruses: antibodies, T cells, NK cells as well as IFN and chemokine production. They showed that lack of activation of APCs and, in particular, lack of IFN production correlate with high virulence. The nucleoprotein appears to play a role in the modulation of IFN production.

They further addressed the immune response to Ebola virus in collaboration with a team in Gabon and the pathogenesis of Nipah virus in collaboration with at team in Lyon and one in Malaysia. Work has been published in very good impact journals such as J. Virol or Emerging Infect. Dis. which are among the best specialized journals in the field.

Basic research work is quite relevant and expected to provide important insight into the virulence factors of arenaviruses that could be tuned down for future vaccine development. Importantly, the search of appropriate in vitro models and the search of relevant in vivo models are included in the project. Originality is not the major strength of the proposed work. This can at least partly be due to the limitations associated with the use of a BSL4 facility. The project is a logical follow-up of previous work. One might regret limited risk taking and/or creativity, which would allow publishing in higher impact journals.

Research associated with reference center activities is more creative and of high quality. The previous head of the reference center has left the team and is not available for the next term.

The team is very dynamic and productive. They recently produced a number of very good primary research papers on top of the reference center activities. The team lists 47 publications. Among them, 13 articles have been published with members of the team acting as first or last authors. The future team leader was particularly productive in the recent years. The outgoing team leader produced much less recently, likely owing to his management activities and also to structural difficulties at BSL-4 in Lyon that need to be solved to create a strong basis for the future research by this team. The report lists one producer for the next funding period. Three producers have contributed to the publication list for the last funding period.

Assessment of the research team's integration into its environment:

The team is strong in networking. The management of the team and the complex intertwining between the BSL4 facility, the reference centers and the Pasteur Institute campus have been organized with some long-term vision. Generally, the work of this team in Lyon is very important since this is the only possibility for Pasteur Institute to have access to a BSL-4 laboratory. The interaction with CIRMF, Gabon, in the field of Ebola virus research has been very fruitful in the past and is expected to thrive in future. It is necessary to sustain the expertise in reverse genetics that has also been contributed by another team within the department.

The reference centers are managed with a limited number of scientists.

Funding was excellent and mostly provided by the scientist who has left the team. The team will be included into the CIRI initiative of infectious disease groups in Lyon which might be a very good opportunity to rise funding.

Assessment of the research team's reputation and drawing power:

The outgoing head of the team was invited to speak at 22 conferences and meetings and the current team leader lists one invited oral presentation.

No particular effort of successful recruitment policy is reported. The ability of the team to recruit researchers needs to be improved.

The team made use of the international Pasteur Institute network.

Assessment of the strategy and 5-year project:

The proposed project is a logical follow-up of previous work. It is not particularly risky or creative but appears to be feasible. Facing the current staffing situation the project needs to be focused to either of the two suggested virus systems. Description of the project is still very broad which does not allow a specific assessment of the strategies envisioned.

A strategy needs to be defined for future funding of BSL4 projects and for access to the facility. This is an important issue.

Establishment of a non-human primate infection model for Lassa fever virus is challenging and may provide important insights into the bases of pathogenicity.

Conclusion:

- *Overall opinion on the team:*

The committee has a first a priori very good impression, but it is difficult to assess given the unusual context of the situation (BSL4 in Lyon and research teams in Lyon and Pasteur Institute). Due to dramatic changes in personnel it is difficult to predict how the different organizational parts of the team (research and NRC activities) will develop. While the perspectives of the research part are very good due to the expertise of the future director in this field, the future of the NRC especially in terms of publication is less clear.

- *Strengths and opportunities:*

- The team has important tools (reverse genetic system) and expertise to be competitive in the field.

- It has a good networking activity

- It performs important surveillance work, including national reference centre activity.

- *Weaknesses and risks:*

- There are potential difficulties linked to the dramatic change in the staff.

- The small team might not be able to conduct all tasks successfully.

- The quality of publications is good but not excellent.

- *Recommendations:*

- The structural basis of the project needs to be addressed.

- Pasteur Institute and the P4 team in Lyon need to finalize their negotiations to provide a secure organizational basis for the project.

- Future integration of the team into CIRI is vital.

Team 16: Molecular Genetics of RNA Viruses

Team leader: Ms Sylvie VAN DER WERF

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	3	3	3
N2: EPST or EPIC researchers	1	1	1
N3: Other professors and researchers	2	1	1
N4: Engineers, technicians and administrative staff * on a permanent position	7 (5,65)	6 (4,65)	
N5: Engineers, technicians and administrative staff * on a non-permanent position	1		
N6: Postdoctoral students having spent at least 12 months in the team	3		
N7: Doctoral students	4		
N8: PhD defended	3		
N9: Number of Habilitations to Direct Research (HDR) defended	1		
N10: People habilitated to direct research or similar	3	4	
TOTAL N1 to N7	**21(19,65)**	**11(9,65)**	**5**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-teames-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

The team is devoted mainly to basic and applied influenza virus research. It is associated with a national Influenza Center and a WHO Reference Laboratory on H5 viruses and SARS-CoV. Studies on the epidemiology, ecology and evolution of animal and human influenza viruses play therefore an important role in the activities of this group. The report period has been marked by the 2009 H1N1 pandemic, and the group made significant contributions to the identification and characterization of this virus. Of particular interest were observations that linked severe disease cases to HA mutations involving a change in receptor specificity. Another field of interest of the group is influenza virus-host interactions at the molecular level. In particular the studies on the interaction of the viral polymerase and the viral ribonucleoprotein with nuclear and cytoplasmic proteins have established the high international reputation of the team. This is documented by a series of very good publications including a review article in Annu. Rev. Microbiol, an original article in Immunity and several articles in J Virol and Plos Pathogen. Other important studies have focused on the role of NA in pathogenicity, the emergence of NA inhibitor resistance, and the development of new NA inhibitors. Overall, the publication list of 69 publications in peer review journals including 27 signed as first or last author is impressive by its size and also by the quality.

Another research interest within the team is on GB virus B (GBV-B), a close relative to hepatitis C virus (HCV). GBV-B causes an acute hepatitis in tamarins, providing a small animal model to study HCV. The team generated a GBV-B chimeria containing HCV IRES that showed selective mutations in the NS5A and 3' nontranslated RNA (NTR) sequences following tamarin infection. This mutation associated with increased fitness *in vivo*, demonstrating complementarity between these regions and 5'NTR. In parallel the team reported that siRNAs targeting the HCV IRES could inhibit HCV replication and GVB-B NS3/4A cleaved MAVS – similar to that observed for HCV protease. These studies have been published in good and very good journals (J. Virol, PLoS Pathogens).

Assessment of the research team's integration into its environment:

The influenza research has a high ecological, public health, and medical impact. The hepatitis studies are more oriented towards basic research, but they also contribute to a better understanding of an important pathogen. External funding of the influenza project is impressive. It is not as extensive with the hepatitis project, but still adequate considering the smaller size of this project.

Assessment of the research team's reputation and drawing power:

Both projects are well integrated into the international scientific scene on their respective fields with a number of international collaborations. Faculty and students are mainly from France. There has been some turnover of staff and it is not clear how this has affected the activities of the team.

Assessment of the strategy and 5-year project:

The future research plans of the team are logical and sound extension of ongoing projects. The influenza research has 2 major goals: (1) The role of genetic diversity as depending on the fidelity of the viral polymerase on evolution and pathogenesis will be analyzed. This project, which will be done in collaboration with team 17 is highly innovative; (2) To elucidate the intracellular trafficking of viral proteins using new imaging techniques. The hepatitis project has 3 aims: (1) Compare the receptor dependent pathways of GBV-B and HCV using lentiviral pseudotypes in collaboration with team 11; (2) To study HCV and GBV-B encoded NS2 structure by NMR with a group a IBCP, Lyon and more generally to study the role of nonstructural proteins in hepacivirus morphogenesis and (3) To study innate and T cell responses in GBV-B infected tamarins by microarray and immune studies in collaboration with a group at NIBSC.

Conclusion:

- *Overall opinion on the team:*

The influenza and hepatitis C virus research is excellent, and the productivity is excellent as well.

- *Strengths and opportunities:*

The influenza research benefits from access to the collection of human and avian isolates available at the public health centers.

- *Weaknesses and risks:*

The research of the hepatitis group focuses on GBV-B whose main advantage as a model for HCV involves in vivo studies with tamarins. Thus, non-human primates are essential for this research, however, the funding for the animal model is not clear. Furthermore, if the animal model is only available at an external site, the leadership of the scientist involved may be threatened.

- *Recommendations:*

The influenza and the hepatitis project operate quite independently, and there are no direct scientific links between them. There must be reasons why the hepatitis project, which may be too small to form a separate team, does not belong to one of the other hepatitis teams at the Pasteur Institute, but such reasons are not obvious to the committee experts. If the hepatitis group were moved to another team, the influenza group would be large enough to continue as an independent team.

Team 17: Viral Populations and Pathogenesis

Team leader: Mr Marco VIGNUZZI

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors			
N2: EPST or EPIC researchers			
N3: Other professors and researchers	4	1	1
N4: Engineers, technicians and administrative staff * on a permanent position	3 (1,75)	3 (1,75)	
N5: Engineers, technicians and administrative staff * on a non-permanent position			
N6: Postdoctoral students having spent at least 12 months in the team	2		
N7: Doctoral students	1		
N8: PhD defended			
N9: Number of Habilitations to Direct Research (HDR) defended	1		
N10: People habilitated to direct research or similar	1	1	
TOTAL N1 to N7	**10 (8,75)**	**4 (2,75)**	**1**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-teames-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

The group studied the biological consequences of the template-copying fidelity of the viral RNA-dependent RNA polymerases of coxsackievirus B3 and Chikungunya virus. The project has been built on and has expanded previous pioneer studies on poliovirus fidelity mutants carried out in the US when the team leader was a postdoctoral student. Coxsackievirus offers several advantages over poliovirus as an experimental system, to study consequences of polymerase fidelity in the natural host for the virus. The research on Chikungunya has introduced copying fidelity in arbovirology, in addition to dealing with a system well implemented in the research activities of Pasteur Institute.

The laboratory has been highly successful, obtaining and charaterizing fidelity mutants of the two new viral systems, and fidelity has been firmly established as an attenuation determinant. Several bottleneck events in the arbovirus life cycle have been identified, and key mutations involved in increased Chikungunya dissemination and transmission have been characterized. For mutant characterization, an infectious clone of Chikungunya has been constructed, and made available to the scientific community.

The results of the laboratory are of high quality. The team leader is last author on a number of excellent impact papers (PNAS, PLoS Pathogens, J. Virol.).

Assessment of the research team's integration into its environment:

The team is well integrated in its environment as shown by a number of ongoing collaborations with other teams at the Pasteur Institute. In addition, collaborations with groups outside Pasteur institute have been highly productive, and collaborations continue at present.

Assessment of the research team's reputation and drawing power:

The team has acquired excellent visibility, as demonstrated by the number of international collaborations, involvement in European consortia, and invitations to participate in scientific meetings.

Assessment of the strategy and 5-year project:

The future plans of this laboratory offer great promise of success on a timely research topic that has implications in key issues of present-day virology. Issues include the effect of population complexity on viral pathogenesis, polymerase fidelity as an attenuation determinant, and the development of virus-specific mutagenic agents as antiviral drugs. In addition, fundamental aspects of viruses at the population level, that the team intends to undertake, include a deeper understanding of the biological consequences of arboviral population heterogeneity, in particular arboviral survival through bottleneck events, or how the host immune system confronts viral populations of different complexity dictated by the fidelity properties of the polymerase.

Conclusion:

- *Overall opinion on the team:*

This is an excellent to outstanding team.

- *Strengths and opportunities:*

The team is pioneer in a timely topic in virology.

- *Weaknesses and risks:*

None

- *Recommendations:*

Continue and expand this line of research

Team: 18 Molecular Retrovirology

Team leader: Mr Simon WAIN HOBSON

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors			
N2: EPST or EPIC researchers			
N3: Other professors and researchers	6	3	3
N4: Engineers, technicians and administrative staff * on a permanent position	3 (2,5)	3 (2,5)	
N5: Engineers, technicians and administrative staff * on a non-permanent position			
N6: Postdoctoral students having spent at least 12 months in the team			
N7: Doctoral students	1		
N8: PhD defended	4		
N9: Number of Habilitations to Direct Research (HDR) defended			
N10: People habilitated to direct research or similar	3	3	
TOTAL N1 to N7	**10 (8,5)**	**6 (5,5)**	**3**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-teames-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

The team head is an international leader in the field of viral, and now cellular, nucleic acid editing. In the last period, the team has made significant insights into the mechanisms underlying the genomic editing of representatives of several groups of viruses, including lenti, non-lenti retro, HBV and herpes, by APOBEC family and related cellular enzymes. This has significance for how we think of the replication of these, and probably other viruses. Importantly, these observations have been extended from in vitro/tissue culture situations to in vivo situations, suggesting roles in viral pathogenesis and host control of virus infection. Perhaps more importantly, the group has shown that the editing activities are not restricted to viral genomes, but can also occur on cellular mitochondrial and nuclear DNA. These findings have implications for oncogenesis, apoptotic destruction of cells with hyper-mutated genomes, and the regulation of DNA damage responses. The 3DPCR method developed by the team has also been transferred to other fields, where it is making a highly useful impact.

The group has published 27 papers in the last period, of which 20 appear to be primary research papers. The quality of publications is outstanding and includes 1 Science, 1 PNAS, 1 Blood, and several field specific journals e.g. J. Virol, J. Mol. Biol. This puts the group at the forefront of research in its domain. Permanent staff made important contributions to successful publication.

Assessment of the research team's integration into its environment:

The team leader holds HIV patents that are important components of the Pasteur Institue portfolio – though details are not given. The PI and one of the staff scientists, through Pasteur Institute, hold a patent(s) on the use of telomerase as a target for immunological improvements in cancer patients. Importantly, they have established a start-up company to develop electroporation methods for DNA vaccination. The team has also developed novel methods that have been widely adopted for specifically amplifying hyper-mutated DNA by PCR.

The group is very well integrated into the Pasteur Institute environment. Numerous collaborations within the institute exist and resulted in common publications.

Since 2008 the group has been awarded 6 grants totaling over 1 million €. Three of these are on-going, though all three expire this year. The team leader and one staff scientist have also been successful in raising in excess of 4 million € for their start up company.

Assessment of the research team's reputation and drawing power:

The national and international recognition of the team leader is highlighted by his election to the Academia Europea (2007). Recent awards and prizes include the French Academy of Sciences Athena prize (2006). He serves or has served on a number of editorial boards (currently EMBO Molecular Medicine).

Although the team leader was trained in the UK, the majority of the team appears to be French.

The group participates in a number of collaborations most of which appear to be with laboratories in Paris or elsewhere in France, though there are connections to laboratories in the UK – in particular the Sanger Centre.

Assessment of the strategy and 5-year project:

The long-term plans of the group now focus on the nucleic acid editing and build on the work developed over the last four years, in particular the hypothesis that hyper-editing of cellular DNA is pro-apoptotic and physiological, while hypo-editing is compatible with cell survival but pathological leading to hyperplasia, dysplasia and ultimately cancer. To this end, one area for focus will be A3A – an APOBEC family member that is induced during inflammation by type I and II interferons.

A3A expression is to be analyzed under various states of stress and linked to cell states such as senescence or cell cycle arrest. They will analyze why A3A alone can target nuDNA when the related A3B, A3C and A3H are co-expressed in the nucleus. They will identify interactors that may regulate A3A activity and have already identified one interactor and suspect there are more to be found. This will be important as a mouse A3A transgenic model failed to show enhanced tumor formation, but the mouse homologue of the interactor negatively regulates human A3A activity. Thus a mouse knocked out for the interactor may show more promising results.

The notion that DNA editing enzymes target not only viral genomes, where they can restrict virus replication, but also affect cellular DNA is highly interesting and potentially important. These ideas are to our knowledge original and warrant further investigation. The choice of projects comes with some risk, but this is offset by the experience and track record of the team leader.

Conclusion:

- *Overall opinion on the team:*

- The team leader has a strong leadership

- The PI selects important research topics

- He has an excellent publication record and high international visibility

- *Strengths and opportunities:*

The group has established novel insights to DNA editing mechanisms, both for viral and cellular genomes. This will puts it in a leading position to develop their hypothesis that cellular DNA editing is a major factor in the development of cancers. Although important and interesting work, the focus is moving away from molecular virology – one question then is how the proposed programme fits with the overall strategy of the Department.

- *Weaknesses and risks:*

The chief risk lies in the temptation to tackle simultaneously the role of APOPBECs in viral infections, normal cellular physiology and cancer. It was not clear from the report how these large and potentially diffuse areas will be prioritized in the next 5 years. This reservation was, however, somewhat allayed by the presentation, in which the team leader made it clear that they will focus on HPV-induced cancer.

Most of the current funding expires in 2012.

- *Recommendations:*

Continue the highly successful work.

Team 19: Arboviruses and Insect Vectors

Team leader: Ms Anna-Bella FAILLOUX

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	0	0	0
N2: EPST or EPIC researchers	0	0	0
N3: Other professors and researchers	3	1	1
N4: Engineers, technicians and administrative staff * on a permanent position	2 (1,5)	1	
N5: Engineers, technicians and administrative staff * on a non-permanent position	1		
N6: Postdoctoral students having spent at least 12 months in the team	1		
N7: Doctoral students	1		
N8: PhD defended	3		
N9: Number of Habilitations to Direct Research (HDR) defended	0		
N10: People habilitated to direct research or similar	1	1	
TOTAL N1 to N7	**8 (7,5)**	**2**	**1**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-teames-de-recherche/Principes-d-evaluation.

• Detailed assessments

Assessment of scientific quality and production:

This is a newly created group, evolving from the successful team "Molecular genetics of Bunyaviruses" after the retirement of its leader. The team is taking arbovirus research in a new direction by studying virus in the actual insect vector, with the particular remit to investigate vector competence. Very few laboratories worldwide have the facilities to do this. The productivity of the group is very good. Key papers on Wolbachia and vector competence, and cycling of RVFV between vertebrate and invertebrate hosts to maintain genome stability, are noteworthy.

Assessment of the research team's integration into its environment:

The team has numerous external collaborations and grants, though generally for small-scale projects. The range of collaborations is indicative of the particular skills available in the team.

Assessment of the research team's reputation and drawing power:

The team has skills in the breeding of different mosquito species, experimental infection with viruses and subsequent analyses of virus dissemination in the insect that are unique not only in France but also in Europe. The team leader is establishing a reputation in the field as evidenced by invited talks. The composition of the current group is rather parochial, largely because it has grown from the previous team within the bunyavirus team. A number of international collaborations have been established.

Assessment of the strategy and 5-year project:

Future projects through Institut Pasteur funding focus on two viruses, Chikungunya and Dengue. As Chikungunya has already reached Europe this is appropriate, and studies on vector competence of "local" mosquitoes are well planned. Dengue is the most important arbovirus, and studies on the potential for emergence in European mosquito strains are also welcome. Continuation of studies of RVFV in mosquitoes will be funded by a new European program. The team has selected 3 viruses to study that are important and relevant to Europe. The proposed studies will shed new light on interactions of these viruses with different mosquito species that will have practical implications for control.

Conclusion

- *Overall opinion on the team:*

This represents an important area of virology at Pasteur. The team is a research leader in this area and appropriate support should strengthen this research area before other institutions in Europe develop their own capacities.

- *Strengths and opportunities:*

The team leader has a unique expertise that is important for the project on vector competence.

- *Weaknesses and risks:*

Breeding and maintaining the different mosquito colonies is very labor intensive and requires considerable technical support.

- *Recommendations:*

To exploit fully the research opportunities of the team, particularly with regard to transmission studies to animals, contiguous BSL3 insectaries and animal facilities are needed.

5 • Grading

Once the visits for the 2011-2012 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 four criteria defined by the AERES and was given along with an overall assessment.

With respect to this score, the research unit concerned by this report (and, when necessary, its in-house teams) received the overall assessment and the following grades:

Overall assessment of the Department of Virology:

Excellente unité à tous points de vue.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
A+	**A+**	**A+**	**A+**

Overall assessment of the **team 1** [**Viral Pathogenesis**]:

Équipe dont la production et le projet sont très bons. Le rayonnement est bon mais pourrait être amélioré.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
A	**B**	**-**	**A**

Overall assessment of the **team 2** [**Regulation of Retroviral Infections**]:

Équipe dont la production est très bonne. Le rayonnement et le projet son excellents.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
A	**A+**	**-**	**A+**

Overall assessment of the **team 3** [**Molecular virology and Vaccins**]:

Équipe dont la production et le projet sont très bons. Le rayonnement est bon mais pourrait être amélioré.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
A	**B**	**-**	**A**

Overall assessment of the **team 4** [**Biology of Enteric Viruses**]:

Équipe dont la production et le rayonnement sont très bons. Le projet est excellent.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
A	**A**	**-**	**A+**

Overall assessment of the **team 5** [**Flavivirus-Host Molecular Interactions**]:

Équipe dont la production, le rayonnement et le projet sont bons, mais pourraient être améliorés.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
B	**B**	**-**	**B**

Overall assessment of the **team 6** [**Genetics, Papillomavirus and Human Cancer**]:

Équipe dont la production et le rayonnement sont très bons et qui ne présente pas de projet propre.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
A	**A**	**-**	**NN**

Overall assessment of the **team 7** [**Oncogenic Virus Epidemiology and Pathophysiology**]:

Équipe dont la production, le rayonnement et le projet sont très bons.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
A	**A**	**-**	**A**

Overall assessment of the **team 8** [**Viral NeuroImmunology**]:

Équipe dont la production et le rayonnement sont très bons. Le projet est excellent.

Grading table:

C1 Scientific quality and production.	C2 Reputation and drawing power, integration into the environment.	C3 Laboratory life and governance.	C4 Strategy and scientific project.
A	**A**	**-**	**A+**

Overall assessment of the **team 9** [**Hepacivirus and Innate Immunity**]:

Équipe dont la production et le projet sont très bons. Le rayonnement est bon mais pourrait être amélioré.

Grading table:

C1 Scientific quality and production.	**C2** Reputation and drawing power, integration into the environment.	**C3** Laboratory life and governance.	**C4** Strategy and scientific project.
A	**B**	**-**	**A**

Overall assessment of the **team 10** [**Pathogenesis of hepatitis B virus**]:

Équipe dont la production, le rayonnement et le projet sont très bons.

Grading table:

C1 Scientific quality and production.	**C2** Reputation and drawing power, integration into the environment.	**C3** Laboratory life and governance.	**C4** Strategy and scientific project.
A	**A**	**-**	**A**

Overall assessment of the **team 11** [**Structural Virology**]:

Excellente équipe à tous points de vue.

Grading table:

C1 Scientific quality and production.	**C2** Reputation and drawing power, integration into the environment.	**C3** Laboratory life and governance.	**C4** Strategy and scientific project.
A+	**A+**	**-**	**A+**

Overall assessment of the **team 12** [**Viruses and RNA interference (VIA)**]:

Excellente équipe à tous points de vue.

Grading table:

C1 Scientific quality and production.	**C2** Reputation and drawing power, integration into the environment.	**C3** Laboratory life and governance.	**C4** Strategy and scientific project.
A+	**A+**	**-**	**A+**

Overall assessment of the **team 13** [**Virus and Immunity**]:

Excellente équipe à tous points de vue.

Grading table:

C1 Scientific quality and production.	**C2** Reputation and drawing power, integration into the environment.	**C3** Laboratory life and governance.	**C4** Strategy and scientific project.
A+	**A+**	**-**	**A+**

Overall assessment of the **team 14** [**Viral Genomic and Vaccination**]:

Équipe dont la production, le rayonnement et le projet sont très bons.

Grading table:

C1 Scientific quality and production.	**C2** Reputation and drawing power, integration into the environment.	**C3** Laboratory life and governance.	**C4** Strategy and scientific project.
A	**A**	**-**	**A**

Overall assessment of the **team 15** [**Biology of Emerging viral infections**]:

Équipe dont la production et le projet sont très bons. Le rayonnement est bon mais pourrait être amélioré.

Grading table:

C1 Scientific quality and production.	**C2** Reputation and drawing power, integration into the environment.	**C3** Laboratory life and governance.	**C4** Strategy and scientific project.
A	**B**	**-**	**A**

Overall assessment of the **team 16** [**Molecular Genetics of RNA Viruses**]:

Équipe dont la production et le rayonnement sont très bons. Le projet est excellent.

Grading table:

C1 Scientific quality and production.	**C2** Reputation and drawing power, integration into the environment.	**C3** Laboratory life and governance.	**C4** Strategy and scientific project.
A	**A**	**-**	**A+**

Overall assessment of the **team 17** [**Viral Populations and Pathogenesis**]:

Excellente équipe à tous points de vue.

Grading table:

C1 Scientific quality and production.	**C2** Reputation and drawing power, integration into the environment.	**C3** Laboratory life and governance.	**C4** Strategy and scientific project.
A+	**A+**	**-**	**A+**

Overall assessment of the **team 18** [**Molecular Retrovirology**]:

Excellente équipe à tous points de vue.

Grading table:

C1 Scientific quality and production.	**C2** Reputation and drawing power, integration into the environment.	**C3** Laboratory life and governance.	**C4** Strategy and scientific project.
A+	**A+**	**-**	**A+**

Overall assessment of the **team 19** [**Arboviruses and Insect Vectors**]:

Équipe dont la production et le rayonnement sont très bons. Le projet est excellent.

Grading table:

C1 Scientific quality and production.	**C2** Reputation and drawing power, integration into the environment.	**C3** Laboratory life and governance.	**C4** Strategy and scientific project.
A	**A**	**-**	**A+**

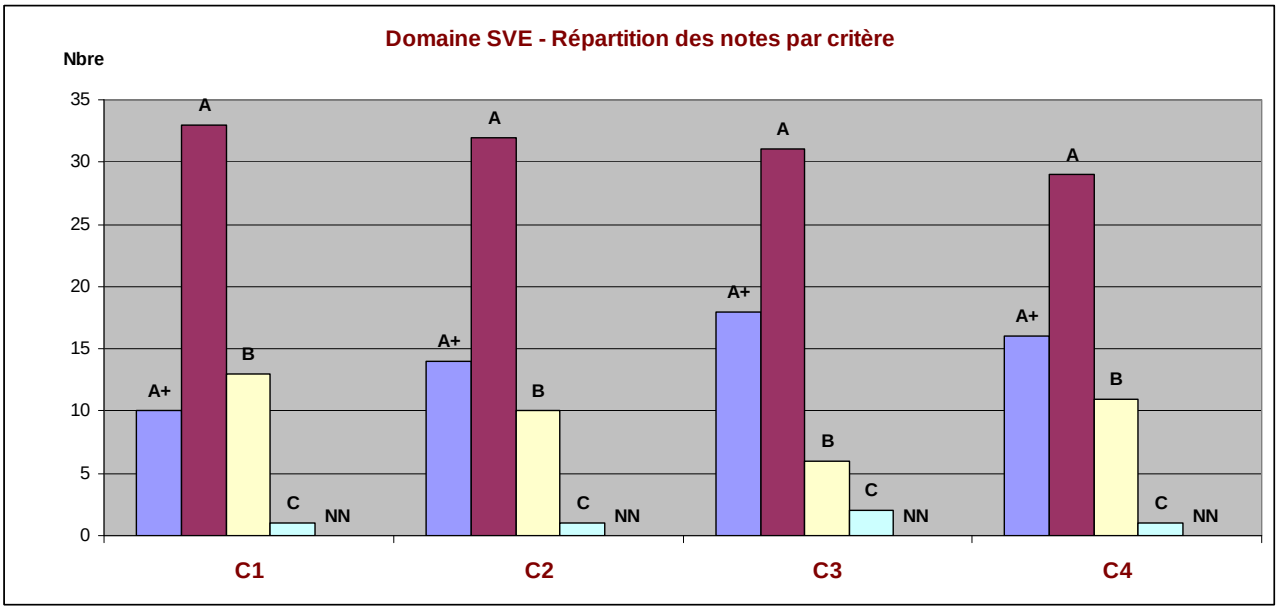
6 • Statistics per field : SVE au 10/05/2012

Notes

Critères	C1	C2	C3	C4
	Scientific quality and production	Reputation and drawing power, integration into the environment	Laboratory life and governance	Strategy and scientific project
A+	10	14	18	16
A	33	32	31	29
B	13	10	6	11
C	1	1	2	1
Non noté	-	-	-	-

Pourcentages

Critères	C1	C2	C3	C4
	Scientific quality and production	Reputation and drawing power, integration into the environment	Laboratory life and governance	Strategy and scientific project
A+	18%	25%	32%	28%
A	58%	56%	54%	51%
B	23%	18%	11%	19%
C	2%	2%	4%	2%
Non noté	-	-	-	-



7 ● Supervising bodies' general comments

Fernando Arenzana
Laboratory of Viral Pathogenesis
INSERM Unit U819

AERES evaluation (march 2012).
OBSERVATIONS

- ***Assesment of scientific quality and production***

1. We acknowledge the positive evaluation of the quality and impact of our work

2. We are surprised that the fact that two new teams emerged from our laboratory seeking for increased scientific autonomy is not explicitly recognized as a positive and fundamental aspect of our accomplished work. This attitude is particularly surprising as the lack of mobility and scientific inbreeding are justly stigmatised as factors jeopardizing the acquisition of full scientific autonomy by our senior investigators. We extend our disappointment to the fact that no comments were made regarding the capacity of our laboratory to promote the recruitment of young scientist (3 during the evaluated period) as staff members by French institutions (2 CR1, INSERM & 1 MC, University).
The last section of the project manuscript (main text) was devoted to explain and comment in detail every point quoted above. Moreover, the same information was summarized in the "EXECUTIVE summary file" requested by the AERES and provided to the committee.

- ***Assesment of the research team's integration into is environment***

1. Regarding the origin of the financial support we want to underline that we obtained financial support from highly competitive grants from the EU (4), Bill and Melinda Gates Foundation and the Mizutani Fundation (Japon). We would like to recall than roughly 80% of our financial support is provided by external grants, which we seek permanently and actively as an essential part of our work. Consequently, we hope that the remark *"financial support was obtained mostly from French agencies"* addressed by the committee, will not be taken as a criticism.

2. Regarding the necessity to find support for our current research "*this year*", we acknowledge the recommendation addressed by the committee. However, we want to make clear that our team relies actually on acquired financial support for conducting each research topic. The funding comes from both competitive grants (ANRS, ANR, SIDACTION, MIZUTANI, LABEX) and recurrent resources (IP, INSERM). The funding, as stated in our documents, cover the proposed research for at least two years. The information was pertinently provided to the committee during the oral presentation and was explicit in the main text of the project manuscript and the table annexed both to the main report and the "EXECUTIVE summary file".

- ***Assessment of the research's team reputation and drawing power***

1. The current and past collaborations were quoted in the main text of the project. They were also exposed in the introduction of the oral presentation to the jury.

2. Regarding the composition of the team and the necessity of replacing the leaving staff scientists, the arrival in our team of Dr. Chakrabarti (head of laboratory, IP) and two collaborators was announced during the oral presentation of the project and was explicitly commented in the "Executive summary file" provided to the committee. This fact seems to have been ignored by the committee. Dr Chakrabarti is an internationally recognised scientist in the HIV field and her incorporation is expected by May 2012.

INSTITUT PASTEUR

Paris, April 16, 2012

Team 2 : "Regulation of Retroviral Infections"
Virology Department

To **AERES Committee**

From ***Françoise BARRE-SINOUSSI***

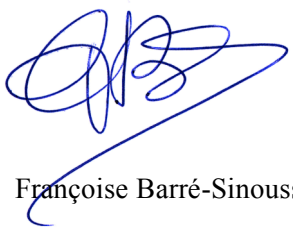
Phone *33 1 45 68 87 30/33*
Fax *33 1 45 68 89 57*
Email *fbarre@pasteur.fr*

Subject *AERES Evaluation Report : Comments of team#2, Virology Department, Institut Pasteur*

Dear AERES committee members,

I would like to thank you for the evaluation of our team and for the accuracy of your report. Our team does not have specific comments on this report, except that we sincerely appreciate the assessments and the conclusion, in particular the recommendations made by the reviewing committee.

Yours sincerely,



Françoise Barré-Sinoussi

Institut Pasteur
25-28 rue du Docteur Roux
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Institut Pasteur

Dr. Francis DELPEYROUX
Department of Virology
Unit : Biology of Enteric Viruses
INSERM U994
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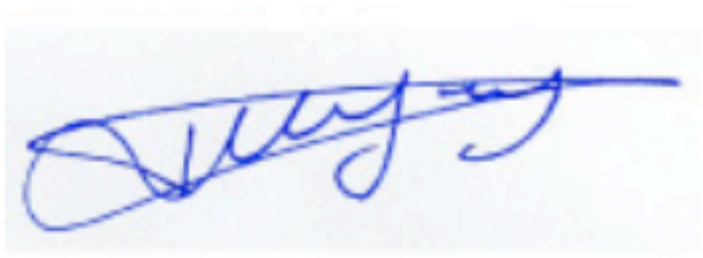
Tel. 33.1.40.61.33.22
E-mail: francis.delpeyroux@pasteur.fr

24th April, 2009

Object : AERES report on unit *Biology of Enteric Viruses*

We greatly appreciate the time the experts took for evaluating the activity of the unit *Biology of Enteric Viruses*. We thank them for their favourable and encouraging comments, and their useful suggestions.



Francis DELPEYROUX

AERES report on Unit :	Department of Virology, Institut Pasteur/University Paris Diderot/UMR_S/UMR
Team 5 :	Flavivirus-Host Molecular Interactions (FHMI)
Affiliation:	Institut Pasteur
Team Leader :	Mr. Philippe DESPRES

Comments on AERES's report about the activities of the Team 5 (FHMI)

First, we would like to thank the AERES committee for their evaluation efforts towards the FHMI research lab. We have carefully examined their critiques and recommandations about our lab activities in the field of arbovirology. The committee recognizes that FHMI has made contributions to the study of arboviral research and is tackling difficult biological problems. It is recognized that during the last three years, the NRC for Arboviruses (that was integrated to FHMI in 2008) has been a valuable public health service. The committee also mentions that the planned research is relevant at understanding arbovirus infections through expertise of the FHMI team and its active collaborations with other academic teams including within the Institut Pasteur. The total funding acquired is recognized to compare favorably with other research labs in Europe. Lastly, the committee states that the list of patents illustrates the effort towards the translation of research findings through production of diagnosis tools and vaccines to combat arboviruses.

However, we wish to provide important corrections and precisions about some remarks of the committee. First, we identify an important mistake in our team workforce. Indeed, there are only two « other professors and researchers » (column 1, line N3 in the Workforce Table) instead of seven as it is wrongly mentioned (see below the modified Table). Thus, it must be understood that the number of publications (29) is mainly associated to two producers. A new senior researcher was recruited in 2012 who is habilitated to direct research (thus there is also a mistake in column 2, line N10 in the Workforce Table, which should read 3 instead of 2, see below the modified Table). Moreover, the international visibility of FHMI lab is real as illustrated by the list of our publications that have received 30 or more citations since the start of our research activities in 2000 (see the table below):

List of publications that have received 30 or more citations	Year	Number of citations
Iglesias *et al.* J.Gene.Med. 8:265	2006	37
Kajaste-Rudnitski *et al.* J.Biol.Chem. 8:4624	2006	44
Catteau *et al.* J.Gen.Virol. 84:2781	2003	46
Navarro-Sanchez *et al.* Arch.Med.Res. 36:425	2005	60
Lucas *et al.* Immunol.Cell.Biol. 81:230	2006	71
Desprès *et al.* J.Infect.Dis. 191:207	2005	82
Courageot *et al.* J. Virol. 74:564	2000	99
Sakuntabhai *et al.* Nat. Genet. 37:507-13	2003	154
Mashimo *et al.* Proc.Na.Acad.Sci. 99:11311	2002	197
Navarro-Sanchez *et al.* EMBO reports 4:723	2003	245
Schuffenecker *et al.* PLoS Med 3(7) e263	2006	374

The NRC activities mainly target the area of medical virology such as diagnostics with a particular emphasis on the survey of emerging arboviroses in France mainland. It is of importance to note that a scientific committee from the French Institut de Veille Sanitaire (InVS), specifically mandated for the evaluation of NRC activities annually, ranked A the activities of the NRC for the years 2008 to 2010.

Furthermore, we feel it is very important to rebut the committe's remarks concerning the lack of evidence for collaboration and research output with the International Network of Instituts Pasteur (RIIP) and with other non-European laboratories. Since 2006, FHMI lab has established fruitful collaborations with non-European partners of the FP-6 programme DENFRAME (that FHMI coordinated) from Mexico (CINVESTAV), Argentina (Foundation Lenoir), Brasil (Foundation Chagas), Thailand (Mahidol University) and virological groups within Instituts Pasteur in Vietnam (Ho-Chi-Minh City), Cambodia, French Guiana, and Senegal. FHMI lab also actively interacts with groups in USA (UTMB, Galveston, TX; USAMIIRD, Fort Detrick, MD; Colorado University, Denver, CO), with Taiwan through the « ANR Blanc programme » ARBOAS, 2011-13), with Australia (Queensland University) through a visiting student (Mertens et al., 2010), with Singapore (Singapore Immunology

Network; Warter et al., 2011). Finally, FHMI collaborated with the Institut Pasteur of Hong-Kong through a visiting PhD student (Kudelko et al., 2012; Brault et al., 2012) and Shanghai through the TRP FlaviLAV (coordinated by FHMI) including two visiting PhD students. Other collaborative projects funded by the ACIP or TRP programmes have been established with the Institut Pasteur of Laos, Nouvelle-Calédonie, République Centrafricaine and Cameroon, and virological groups in French Polynesia (Institut Malarde).

Another important clarification pertains the mission of POLARBO, the newly created entity in FHMI. Because we consider that it is essential to retain virologists who have an excellent experience in medical arbovirology, we established the POLARBO team that includes two technicians and one biologist originally working in the NCR for Arboviriuses. POLARBO should enable efficient use of available arbovirological resources and offers exceptional opportunities to directly translate academic research discoveries into clinical and viral diagnostic tools. The current R&D projects we are developing between POLARBO and SMEs in diagnosis or vaccinology demonstrate how beneficial such collaborations can be. Moreover, an added value of POLARBO is to bring greater interaction between basic virological research and medical arbovirology in training the next generation of medical arbovirologists within the RIIP and elsewhere (e.g., EU FP-7 EPISOUTH *Plus* programme). A representative of the WHO's management board (Geneva, Switzerland) has recently validated the strategic approach of POLARBO that matches that of WHO by the nomination of FHMI along with two other laboratories at the Institut Pasteur in Paris as a formal Collaborating Center dedicated to arbovirose and viral hemorragic fevers. Finally, the daily work on arboviruses by FHMI (academic research and POLARBO) imposes the use of a laboratory that complies with all the safety rules including the handling of pathogens Class 3. Since 1993, the research group of the FHMI lab has been housed on the first floor of the Borrel building that is far from offering all up-to-date safety requirements, due to its recognized dilapidation.

In conclusion, we feel that important aspects about our lab integration in its environment, as well as its reputation, international visibility and scientific production have not been entirely taken into account.

Institut Pasteur

Unité de Génétique,
Papillomavirus et Cancer Humain

Centre National de Référence des
papillomavirus humains

16/04/2012

After reading the report on the activity of the Unit, I have no comment to make

Michel Favre

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cnrhpv@pasteur.fr

Institut Pasteur

Unité
« Hépacivirus et
Immunité Innée »
Directeur : Dr. Eliane MEURS

Paris, le 02/10/12

We thank the members of the AERES committee for their remarks. We are pleased to note that the committee recognized the importance on our research on HCV and lipoproteins, on the role of PKR as a pro-HCV agent and the importance in studying the role of HBx on HBV infection.

We would like to make some corrections. First, our funding at the time of the evaluation was 390,000 € and not 290,000 €. Second, the assumption that we have limited collaboration with « Institut Pasteur » colleagues was not correct. We have had collaborations with at several 7 groups within the Pasteur Institute and collaboration with the International Network of Pasteur Institute and some of these collaborations are still going on.

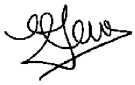
Regarding our project on the role of PML nuclear bodies in HBV infection, the committe mentionned some recently published work on this subject. We want to point our that these publications are contradictory and performed in artificial conditions, using HepG2 cell lines stably expressing the integrated HBV genome. In contrast, our strength is to use real conditions of infection with HBV using HepaRG cells. Only this approach can bring valuable informations on the mechanisms regulating HBV transcription in the setting of a natural infection.

Regarding our different projects linked to HCV evasion, the committe indicated that not enough explanations were given. We apologize for this but the space limitation of the report did not allow to explain in details all the technical procedures.

In the section « Overall opinion of the team », we respectfully disagree for the use of middle-ranking journals over the 2007-2012. In this section, our publications in Plos Pathogens and Science Signalling should have been highlighted as they represent an important recognition of our contribution to HCV and HBV research.

Regarding the assumption of the committee that « team functions as an aggregate of 3 independent research laboratories with minimal connection », we want to answer that we do not consider ourselves as an « aggregate » of three independent labs. Rather, we are working on different aspects of the interaction of hepatotropic viruses with their common host cell. The day-to-day confrontation or our approaches: HCV and lipid metabolism, HCV and innate immunity signaling, HBV and epigenetics, is generating a fruitful exchange that has a common goal : increase immunity against these two viruses.

Best regards



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Instituts thématiques

Inserm

institut national de la santé et de la recherche médicale

INSTITUT PASTEUR

Centre de Recherche Necker INSERM U 845
Institut Pasteur

Pathogenesis of hepatitis B virus, Team 10

Point by point responses to AERES committee

Assessment of scientific quality and production:

The productivity is average for a small group. The publication record for the past few years is modest both in the number (10 peer reviewed publications deriving from direct work of the team).

Comment: Publication number should be considered according to number of people in the team. From 2007 to September 2010 the team consisted of only 5 members. A staff scientist joined the group with 4 additional members in September 2010.

Assessment of the research team's integration into its environment:

However, it is not clear to the experts of the committee how interactive the group is with colleagues at Institut Pasteur, the lack of communication with the other team working on HBV is noteworthy.

Comment: The team is collaborating with colleagues from the Virology (Unité des Régulations des Infections rétrovirales) and Immunology (Unité de Biologie des Populations Lymphocytaires) Departments. The team leader is coordinator of a program supported by a grant from Institut Carnot that involves 3 different units of the department. The work on HCC and liver inflammation is done in collaboration with members from units of other departments (Unité de Recherche Cytokines et Inflammation, Unité d'Histopathologie humaine et modèles animaux, Unité Défense Innée et Inflammation and plate-forme Transcriptome et Epigénome).

There is no lack of communication with the other staff member working on HBV in the Hepacivirus group. The Team 10 "Pathogenesis of hepatitis B virus Lab" was not able to welcome this staff scientist due to a space limitation and to a decision from the scientific board of Institut Pasteur. Both teams are located in the same building and scientific exchanges and discussions are frequent.

Assessment of the research team's reputation and drawing power:

It is difficult for the committee to judge based on the material provided. The executive summary only lists five invited lectures over 2007-2011 period for the team leader and no mention is found about editorial board membership, grant committee participation etc.

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Comment: due to the limited space available, such information was not provided in full. The team leader is a member of several committees for grant evaluation at national level (ANRS, ANR Emergence, RPIB) and at international level (The Wellcome Trust UK, The Korea Research Foundation, WHO, Initiative for Vaccine Research (IVR), The Merieux Research Grants, Le Fonds National Suisse de la Recherche Scientifique, The Italian Association for Cancer Research, The genesis Oncology trust, New Zeland, The Helmholtz Association, Germany).

Overall opinion on the team:

The group is at a transition point with the retirement of its head in three years and contingency plans were not provided. Nevertheless, the future plans will continue to build on the path defined by previous studies and collaborations. The probability that the group will continue to do solid research is high.

Comment: Funding from EU has been obtained for the staff scientist working on HCC for up to 2015. This staff scientist is expected to apply for the creation of a new unit from Institut Pasteur at the next call.

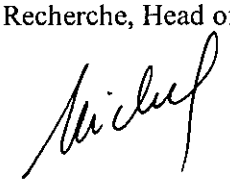
Weaknesses and risks:

The value of the mouse models for human hepatitis and cancer remains to be seen. However, one questions just how far this work can be taken in terms of making valid comparisons with human disease, when there is abundant clinical material and other arguably more relevant models of hepadnavirus pathogenesis available.

Comment: The study on interaction between HBV-infected liver cells and cells from immune system required samples of liver biopsy from patients. Such material is not available in France, as biopsies are no longer performed in most European countries.

The analysis of first steps of liver carcinogenesis starting from inflammation and beyond cannot be performed on human material as most tumor samples are taken from patients at advanced stages of liver carcinoma and not at pre-tumoral stages.

Dr. Marie-Louise Michel
Directeur de Recherche, Head of Laboratory



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Institut Pasteur

G5 Viruses and RNAi

Maria Carla Saleh
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Paris, April 15th, 2012

Dear AERES Evaluation Committee,

I have received and read with great pleasure your assessments and conclusions on our current and future scientific program.

Regarding your concerns for lack of accessibility to BSL3 facilities, I will take special care to make this recommendation reach the appropriate decision-making people at the institute.

I want to thank you for such a positive evaluation and I hope we will be able (as a team and as individuals) to keep up the current pace of research.

Best regards,

Maria Carla Saleh

Institut Pasteur

Paris, April 25 2012

Unité Virus et Immunité
Département de Virologie
Pr Olivier Schwartz

Observations from the representatives of STAFF SCIENTISTS to the AERES committee :

« Questions specifically related to the Department:
The new JDV and the International Seminar Series have been good initiatives to improve the scientific life of the department, but a bigger effort is needed to enhance inter-entities collaborations.
The scientific council of the department has turned into a hollow element of the department's life. The CS is neither decisional, nor consultative and, because the meetings are infrequent, nor even informative (see for instance the nomination of the future Head of the Department).
Better coordination for the election of consensual candidates (e.g. COMESP)

Evolution of scientific carrier
There is a generalized feeling of lack of evolution perspectives.

- *Difficulty to assume responsibilities, in particular in small-size structure*
- *Feeling of lack of confidence and support for Heads and Direction:*
  - *Low number of promotions to DR*
  - *No recognition of work of Team Leaders*
  - *Lack of internal calls for creation of new Units (2 units in 5 /6 years)*
  - *In contrast, use of resources for new international calls to the detriment of support for scientists already performing excellent science at IP*
  - *Moreover, most staff scientist at IP can not be candidates to lead G5 because of very restrictive time since getting PhD*

Administrative note (n0080)
This note reasserts the ratio of ITA per scientist at IP to 1 per 8 (only 17 of 60 ITA would be assigned to an entity). Such quota would negatively impact, directly and indirectly, in the quality of the research developed at IP. This personal is key to: assure the memory of the lab; develop long-term based projects not always aimed to ensure publications; formation and transmission of savoir faire to non permanent personal. In addition it would imply yet another increase in the administrative tasks of staff scientists:

- *HSQE, quality and lab management conducted by ITA*
- *New external applications for further funding to keep ITA. International calls because National calls not adapted."*

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Paris, April 15 2012

Unité Virus et Immunité
Département de Virologie
Pr Olivier Schwartz

To the AERES SVC

Thanks for the comments on my Unit. I feel that the project part is too detailed, and gives too much information on our future goals. I would not appreciate that our potential competitors find these information freely available on internet!! Please can you remove experimental, technical and scientific details in the part below? I have used the visualization mode of correction to highlight my suggestions. Thank you for your understanding of the situation.

Sincerely

Olivier Schwartz
Director of Virus & Immunity Unit
Director of the Virology Department

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Institut Pasteur

Unité de Génomique Virale et Vaccination
Frédéric Tangy

Paris, April 20, 2012

Frédéric TANGY E14-Observations

We thank the reviewers for their helpful comments that will be taken into account for the future of our research activities. However, we would like to make some observations on the report.

Number and quality of publications: The reviewers misunderstood the workforce and composition of the team during the reporting period. The number N3 (other professors and researchers) on 06/30/2011 was 1 and not 4. Indeed, two additional permanent scientists recently joined the Unit (2010 and 2012), and their publications were reported in the reports of their previous Units (URM and UGMVA). Consequently, the mentioned 44 publications generated by UG2V correspond to the production of 12 FTE, including only 3 permanent research scientists. Thus, we completely disagree with the reviewer opinion on the judgment that publication track record is "modest relative to the size of the group".

Concerning the quality of publications, we disagree with the idea that virology of infectious diseases journals, such as JVI, JID are "lower profile specialty journals", as they are the journals dedicated to virology. Moreover, the proteomic program of the lab that was ignored by the reviewers generated some nice articles (MCP, PLoS-Path, NAR). The reviewers acknowledge the very high capacity of the Unit to develop translational research projects (such as clinical trials). This is a clear assessment of our research interest in public health through development of innovative vaccines and therapies. This perfectly matches with the international and traditional positioning of Institut Pasteur. Although such research activity may not allow publication in top ranking broad readership journals, we still consider it as our mission and expect that the Institut Pasteur Direction shares this point of view.

Composition of the team: On page 51 in "Assessment of the research team's reputation and drawing power", the reviewers write: "most members of the team have received their training in France". However, more than one third of the team (7/18) grew up in foreign countries at least up to high-school studies, 5 graduated abroad from France, and 3 did their PhD or their post-doc out of France.

Research program: according to the reviewers, "much of the focus in the 5-years plan is around refinement of the Measles Vaccine-based vaccine vector". Reviewers completely blindfolded a major research program that aimed at developing tools for the high-throughput analysis of virus-host protein-protein interactions (I-MAP). This highly challenging program was directed by the Unit and involved collaborations with 11 Units from the Virology Department and 3 other Units on the Campus over the last 7 years. This program generated 21 publications that represent half of the Unit production over the report period. The Chikungunya virus initiative (mentioned by the reviewer) greatly benefited from this I-MAP program cited as a model in "recommendations" in the Virology Department report, where again the I-MAP program is not cited at all. We really do not understand how reviewers could omit the I-MAP program in the UG2V report.

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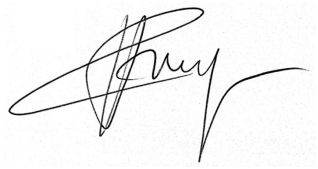
Conclusion (Weaknesses and risk): The comment of the reviewers considering “the absence of a hypothesis in many of the discovery projects” is really gratuitous. Apparently, major international pharmaceutical companies (GSK, Sanofi, Themis, Trangene) consider that these projects have enough robustness and potential to engage high amount of money into collaborative R&D programs that greatly benefit to all Pasteur Institute through requested overheads.



Frédéric Tangy

Team #15, Unit of Biology of Emerging Viral Infection

We first thank the Committee for his overall opinion about our team. We just want to add a few comments about some points raised by the Committee.

-We agree with the necessity to rapidly increase the number of scientists. This is a priority for us and we will do our best to attract additional post-doctoral researchers, M2 then PhD students, and importantly, a supplementary permanent senior scientist. This latter position should ideally be held by a molecular biologist/virologist. Two applications for post-doctoral fellows are currently submitted and we will discuss with the Pasteur Institute to find a solution for the permanent position.

-Concerning the research project, the lack of creativity and the limited risk taking is due to the low number of scientists present in the Unit when the project was written. The increase of the scientific staff size will allow diversifying investigations about Lassa fever and proposing more original and risky projects. In addition, the non-human primate model of Lassa fever will provide original and important insights into the pathogenesis of the disease. As suggested by the Committee, with regards to the current limited staff, we will focus our investigations on Lassa fever.

-We are aware of the urgent need to obtain financial support to fund the projects proposed for the five next years. This point is another priority for us and we are actively searching supports. Two proposals are currently submitted: one to fund the primate experiments (ANR) and the other to the PTR call for proposal. Two post-doctoral fellows are included in these proposals. Finally, a research project associated to the NRC for FHV has been submitted to the ACIP call for proposal. Importantly, UBIVE is one of the partners of the LABEX 'Ecofect', which has been recently accepted.

-We are not worried about the effects of the personnel changes on the development of the different parts of the Unit. On the contrary, we think that the reorganization in three parts will allow developing both reference and research activities. The Head of the Unit (and therefore of the fundamental research part) has a 16-year expertise in FHV (Ebola and Lassa viruses). He is also the Head of the NRC for VHF, in association with the P4 Laboratory team. This joint venture between Pasteur Institute and Inserm that associates an expert team, the BSL4 facilities, and an international network, will allow developing the activities and strengthening this NRC. Finally, the new Head of the NRC for Hantavirus has a long-term expertise in field virology, diagnosis, and epidemiology. After four months of activity, the new organization of both NRC is fully functional and expending.

Concerning the question of the Committee about the future publications of NRC compared to the past activity, it is important to note that most of NRC publications for the past 5 years were related to the Arbovirus part. Activities and staff related to Arboviruses (2 PharmD and 1 MD, H. Zeller, I. Schuffenecker, and M-C Georges Courbot) have left the Unit since 2008. Therefore, as Arbovirus diagnosis represented the main part of NRC activity, the future production will be consequently less significant.

-The problem of relationship between the P4 laboratory Inserm team and UBIVE is clearly behind us. Indeed, the previous problems about holding and accessibility of BSL4 viral strains have been clarified between both Heads of the teams but also at the level of Pasteur and Inserm Directors. Another important problem between the precedent Head of UBIVE and the P4 team was the lack of collaboration for VHF reference activities. This concern is also clarified, as the NRC for VHF consists of both teams since January 2012, with the Head of UBIVE as Director of the NRC and a PharmD from the P4 team as Deputy Director. This new organization, formally agreed by InVS, allows close and

friendly collaboration between both teams and brings complementary skills and means to the NRC. Importantly, close collaboration between both teams has also been established for the research activities, as illustrated by the participation of the P4 team as a partner in the Lassa primate model project. Finally, discussion is ongoing between Inserm and Pasteur Institute to finalize the agreement about BSL4 accessibility to UBIVE and to negotiate a cheap access to the facility. Therefore, we are particularly optimistic about this concern.

-Finally, we agree with the Committee that the future integration of the team into CIRI is vital. Both Pasteur Institute and Inserm show a strong motivation to make UBIVE an important member of the CIRI. The Head of UBIVE animates one of the five scientific objectives of the CIRI, and the Pasteur Institute should be a founding member of the CIRI. Therefore, the integration of UBIVE into the CIRI will be effective without any doubt.

Sylvain Baize

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We thank the Committee for its helpful comments and would like to convey to the reviewers the following observations on the report.

We would like to highlight that the research activities of the team on hepatitis viruses are not restricted to GBV-B, but also focus on HCV and comparative studies of these two hepaciviruses, as attested by publications of the 2007-2011 period and ongoing studies. We feel that this may be stated more clearly in the report.

We do appreciate the concerns of the Committee with respect to the fact that housing of small primates is not available at the I.P. We would like to stress, however, that nonhuman primate studies have been carried out under the leadership of the I.P. scientist in partnership with several collaborators who manage breeding colonies of small primates (SFBR, San Antonio, USA; CdP, ULP, Niederhausbergen, France; NIBSC, Potters Bar, UK). These studies (including ongoing projects) have been successfully funded by the NIH, ANR, and ANRS. The team will seek to pursue the animal studies planned under similar settings.

Hoping that these observations can be taken into account,

Sincerely,

Sylvie van der Werf

INSTITUT PASTEUR

Laboratory "Arboviruses and Insect Vectors"
Department of Virology

Paris, April 13th 2012

Dear Committee members,

I would like to thank the committee members for their participation in the AERES evaluation of the Department of Virology and for their constructive and critical comments. We have carefully read the AERES report and have no major comments to make in reply to the evaluation report on our laboratory.

Sincerely,

Dr Anna-Bella FAILLOUX
Leader of the Laboratory

Alain ISRAËL
Directeur de l'Evaluation scientifique
Institut Pasteur