CRIC - Centre de recherche sur les infections chroniques

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on unit:

Research Center on Chronic Infections

CRIC

Under the supervision of the following institutions and research bodies:

Nouvelle Université de Montpellier

Centre National de la Recherche Scientifique - CNRS

Institut National de la Santé Et de la Recherche Médicale - INSERM

Établissement Français du Sang

January 2014

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

Department for the evaluation of research units

On behalf of AERES, pursuant to the Decree of 3 november 2006[1]*,*

- Mr. Didier HOUSSIN, president
- Mr. Pierre GLAUDES, head of the evaluation of research units department

On behalf of the expert committee,

- Ms Elisabeth MENU, chair of the committee

[1] The AERES President "signs [...], the evaluation reports, [...] countersigned for each department by the director concerned" (Article 9, paragraph 3 of the Decree n ° 2006-1334 of 3 November 2006, as amended).

Evaluation report

This report is the result of the evaluation by the experts committee, the composition of which is specified below.
The assessments contained herein are the expression of an independent and collegial deliberation of the committee.

Unit name:	Research Center on Chronic Infections
Unit acronym:	CRIC
Label requested:	UMR_S, UMR
Present no.:	
Name of Director (2012-2013):	Mr Christian DEVAUX
Name of Project Leader (2014-2018):	Mr Philippe VAN DE PERRE

Expert committee members

Chair: Ms Elisabeth MENU, Institut Pasteur, Paris

Experts:

Mr Charles BANGHAM, Imperial College, London, United Kingdom

Ms Cécile BEBEAR, Université de Bordeaux

Mr Philippe BENAROCH, Institut Curie, Paris

Ms Hélène DUTARTRE, Université Claude Bernard Lyon 1 (representative of INSERM)

Mr Jean-Jacques LETESSON, Université de Namur, Belgique

Mr Gilles MIRAMBEAU, Université Pierre et Marie Curie, Paris

Mr Olivier NEYROLLES, Université Paul Sabatier, Toulouse (representative of CNRS)

Ms Gabriella SCARLATTI, University of Milan, Italy

Mr François SIMON, Université Paris Diderot, Paris

Ms Astrid VABRET, Université de Caen Basse-Normandie (representative of CNU)

Scientific delegate representing the AERES:

Ms Sophie DE BENTZMANN

Representatives of the unit's supervising institutions and bodies:

Mr Michel DESARMENIEN (Representative of Doctoral School n°168)

Mr Olivier GARRON, Établissement Français du Sang

Mr Bruno LUCAS, CNRS

Mr Jacques MERCIER, Université Montpellier 1

Ms Stéphanie POMMIER, INSERM

Preamble:

The proposed Research Center on Chronic Infection (CRIC) will be composed of several research teams from different units of Montpellier: the UMR 5236 (CPBS), the INSERM U1058, the TransDiag unit (actually EFS, Etablissement Français du Sang/French Blood Service) and MPNTT team currently in the UMR 5235 (DIMNP: Dynamique des Interactions Membranaires Normales et Pathologiques, director: Ms Catherine BRAUN-BRETON).

For the parts 1, 2 and 3 of this report, CPBS and INSERM U1058 are evaluated separately except for the last item "Assessment of the five-year plan and strategy" which is treated at the end for the common project of the CRIC.

The MPNTT team and TransDiag becoming DTI team are evaluated in the part 4, team-by-team analysis.

1 • Introduction

History and geographical location of the unit

- **UMR 5236 / CPBS**

The CPBS was created in Montpellier in 2007 from the combination of several research teams from different units in Montpellier: (UMR 5121 CNRS-UM1; UMR 5160-CNRS-BioRad-UM1-UM2; UMR 5539 CNRS-UM2; U 431 Inserm-UM2) leading to a center of 11 teams involved in infectious diseases. One of the teams left in the early period. The teams were located in 3 different sites but were gathered in December 2010 in a new research building located on the CNRS campus of the « Route de Mende » (financial support from the CNRS, the government and the Region Languedoc Roussillon). They benefited from the interactions with teams from neighboring laboratories (CRBM and IGMM) as well as from mutualized services (communication, web site, logistics etc…) and high-technology facilities including biosafety level-3 (BSL-3) laboratories and an imaging facility platform (MRI).

The CNRS has approved the renewal of the CPBS in January 2011 with some restrictions: one team lead by a DR2 CNRS had to be subjected to mid-term review (former team E7), 2 other teams led by a CR1 INSERM and a CR1 CNRS were not created and had to reorganize. This decision led to the departure of the CR1 INSERM team in June 2012 to a local INSERM unit specialized in cancer research, while the team led by the CR1 CNRS was maintained at the CPBS upon request of the CPBS Director (former team E6). At the mid-term evaluation (end of 2012), both teams E7 and E6 were granted with a positive scientific opinion from the INSB. One DR2 CNRS, who lead one of the CPBS teams (former team E4), left the CPBS in early 2011 and a CR1 INSERM took over the management of this team. Two new teams arrived (former teams E2 and E10), the former team E2 led by a young scientist with an ATIP/Avenir program (February 2011) which will be the CBBI team in the CRIC project, and the former team E10 lead by a CR1 CNRS from the ENS Lyon and an IR1 CNRS from the Institut Fresnel (Marseille) (January 2012). The CPBS is at the moment of the onsite visit composed of 10 research teams specialized in virology, bacteriology and pharmacology. The permanent staff of the CPBS mainly belongs to CNRS.

In addition to the CPBS organization, the CEMIPAI platform is being established. This platform is dedicated to the study of infectious agents and the screening of molecules with antibiotics or antiviral properties. In parallel to the development of the CEMIPAI BSL-3 platform, a CEMIPAI service has been set up in particular a bioinformatics service with two bio-scientists (professors from UM1 and UM2).

- **INSERM U 1058**

The INSERM U 1058 unit was created in January 2011 by merging a university research team (EA 4205) working on HIV pathogenesis, transmission and prevention and a group of a dermatology unit (Institut Universitaire de Recherche Clinique, IURC). The unit members are located mostly at the Université Montpellier 1 (UM1) site, faculty of pharmacy but also at the University Teaching Hospital (CHRU) Laboratories.

Management team

- **UMR 5236 / CPBS**

The CPBS in under the scientific and administrative supervision of a management team composed of a director (Mr Christian DEVAUX), a deputy director (Mr Stephan KÖHLER) assisted by and a general secretary. The management team relies on different specialized groups to gather opinions prior to important decisions: the laboratory board, the board of team leaders, the health and safety committee and the group of prevention assistants. The management team also supervises and consults the support team responsible for administrative and financial issues.

The Director (PhD, Research Director CNRS) and the deputy Director (PhD, Research Director INSERM) are well recognized scientists nationally and internationally respectively in the field of immuno/virology and bacteriology. The Director is also in charge of the CEMIPAI platform while the deputy Director is leading a team. The Director was also highly involved in national duties (councilor and then Director of life science and health at the French ministry for Education and Research; member of the governance board of several national institutions, director of research programs and capacity building at AIRD agency).

- **INSERM U 1058**

Mr Philippe VAN DE PERRE, (MD/PhD, PU-PH), is the director of this unit. He is also vice president (in charge of research) of the CHRU Montpellier Directorate and member of the scientific committee of the faculty of medicine, at Université Montpellier 1. He has been very active in the infectious disease field for many years and has acquired an excellent national and international recognition. He is very dynamic and successful to establish collaborations and is involved since many years in programs with resource limited countries.

There are no separated teams in the unit but three different domains of research. Each domain is led by a methodologist or a clinician and a researcher.

AERES nomenclature

- **UMR 5236 / CPBS**

SVE1_LS6 Immunologie, microbiologie, virologie, parasitologie

SVE1_LS7 Epidémiologie, santé publique, recherche clinique, technologies biomédicales

SVE1_LS1 Biologie Moléculaire et Structurale, Biochimie

SVE1_LS2 Génétique, génomique, bioinformatique

SVE1_LS3 Biologie cellulaire, biologie du développement animal

SVE1_LS4 Physiologie, physiopathologie, biologie systémique médicale

- **INSERM U 1058**

SVE1_LS6 Immunologie, microbiologie, virologie, parasitologie

SVE1_LS7 Epidémiologie, santé publique, recherche clinique, technologies biomédicales

Unit workforce

Unit workforce	UMR 5236/CPBS Number at 30/06/2013	INSERM U1058 Number at 30/06/2013	TransDiag Number at 30/06/2013	Number at 01/01/2015
N1: Permanent professors and similar positions	5	14	1	22
N2: Permanent researchers from Institutions and similar positions	18	1	3	26
N3: Other permanent staff (without research duties)	11	7	3	25
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)				
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	5	2	2	12
N6: Other contractual staff (without research duties)	2	7	2	7
TOTAL N1 to N6	**41**	**31**	**11**	**92**

Unit workforce	Number at 30/06/2013	Number at 30/06/2013	Number at 30/06/2013	Number at 01/01/2015
Doctoral students	22	9	1	
Theses defended	19	7	1	
Postdoctoral students having spent at least 12 months in the unit*	12	3	2	
Number of Research Supervisor Qualifications (HDR) taken	7	3	1	
Qualified research supervisors (with an HDR) or similar positions	19	11	2	44

2 • Assessment of the unit

• UMR 5236 / CPBS

Overall opinion about the unit

The CPBS was created in Montpellier in 2007 under the supervision of Mr Christian DEVAUX (PhD/ DR CNRS). After some restructuring, the unit (about 76 people) is now divided in 10 teams lead by 1 or 2 team leaders. During the evaluated period, the unit performed excellent quality fundamental research in the field of virology, bacteriology and anti-infectious pharmacology. Several teams are national leaders of their field (antisense proteins, autophagy in HIV, gag assembly, Coxiella, Brucella). The unit is very active in training and has a strong attractiveness. During the period, 6 scientists obtained a permanent position within the unit. The unit received grants from national and international funders and some of the teams have strong interaction with private companies such as DEINOVE. The level of collaborations is very good and the unit participates in several national or international networks. The CPBS is an important player in infectious disease research in the région Languedoc Roussillon.

Strengths and opportunities

- the CPBS provides an excellent quality of fundamental research in the field of virology, bacteriology and anti-infectious pharmacology. Several teams are national leaders in their field (PPRIantisense proteins, for Autophagy in HIV, MDVA for gag assembly, CBBI for Coxiella, BPAIS for Brucella);

- the CPBS represents a high potential for a critical mass of researchers concerned by chronic infections (viral and bacterial);

- the CPBS benefited from an excellent scientific environment with the proximity to 2 other centers (CRBM and IGMM);

- the CPBS has a strong attractiveness, illustrated by the incorporation of new talented scientists either as team leader (team leader of CBBI team) or through recruitment (INSERM-CNRS);

- the CPBS has the potential to develop through recruitment of new talented group leaders;

- the CPBS has been involved in biotech start-ups and collaborative projects for the development of new technologies and new antibiotics;

- the CPBS has access to and participated in shared services;

- the CPBS has been very active in scientific animation and education.

Weaknesses and threats

- there is a need to strenghten clinical research and to develop translational research projects;

- under the current mandate, low level of internal collaborations was noticed;

- there are some financial concerns, since there was no more financial contribution from the universities to the CPBS infrastructure since the move despite the increasing cost of the infrastructure. This means that the capacity of the CPBS to support research is decreasing on the recurrent budget allocated by the CNRS because a part of the research budget is used for infrastructure. Biosafety measures and the operation of the CEMIPAI platform (including salaries) are also very expensive. There is real risk of being unable to support infrastructure of the CPBS and of the CEMIPAI platform;

- funding might be an issue relatively rapidly for a few teams;

- regarding the outreach of CPBS, the website is not really attractive.

Recommendations

- there is an urgent need to increase fund raising, in particular from industry;

- the CPBS has to increase applications to international organizations and to participate to European consortia;

- the CPBS has to increase visibility and to improve communication;

- the policy to favour interactions between the teams at all levels to promote an active scientific life must be a priority in particular to strengthen projects in same fields and thus to promote higher IF publications;

- the publication policy must be more aggressive to publish in high impact factor journals;

- the CEMIPAI platform position in the unit has to be clarified in term of project, funding and personal and the experts committee recommends that the organization and functioning of the CEMIPAI platform clearly distinct from the center.

• INSERM U 1058

Overall opinion about the unit

The INSERM U 1058, created in January 2011 under the supervision of Mr Philippe VAN DE PERRE (MD/PhD, PU-PH), is dedicated to translational research on infectious diseases and international health. Three topics are developed in particular:

1) transmission and prevention of the HIV infections;

2) interaction between HIV and other infectious agents;

3) viruses with mucocutaneous tropism.

The unit is currently composed of about 40 people. The scientific quality of the unit is excellent and internationally acknowledged. Major achievements are their crucial role in clinical trials to prevent mother to child transmission through breastfeeding. In term of fundamental research, they have made important contributions in the understanding of the mechanisms of HIV-1 transmission by breastfeeding and the characterization of the HIV reservoir in the genital compartment. The academic reputation of the unit is outstanding. The scientific activities of the unit are extremely attractive for new people and new teams. They have a very large network of regional, national and international collaborations with a very active partnership in particular with limited resource countries. Their activities are perfectly integrated in the strategic plans of the région Languedoc Roussillon for infectiology. The unit has also a very strong partnership with the CHRU of Montpellier. The director plays a crucial role in promoting clinical research in Montpellier. The unit has very strong support and recognition from all the local institutions. The unit is very active in training and teaching in particular for people in developing countries. The unit is also highly successful in getting important funding including from international organizations.

Strengths and opportunities

- the unit is involved in translational research (bench to bed and vice versa) and this is supported by added value of fundamental research to clinical research, thus leading to translation into public health interventions;

- the unit has a strong partnership with the CHRU;

- the projects of the unit are fully inserted in the regional strategy;

- the unit has managed a number of projects with limited resource countries in sub-Saharan Africa and Asia essentially and has built a unique network of workers and patients in developing countries;

- the unit is the world leader in infectious disease epidemiology and prevention;

- there is a strong partnership in several scientific networks;

- there is an important and secure funding for the coming years;

- the unit has constituted a high number of sample collections and worldwide cohorts.

Weaknesses and threats

- the basic research in immunology and infectiology beside epidemiology is not enough developed;

- the unit leader and unit members are fulfilling many functions (clinic, clinical trials, teaching, leading the unit…) that may impede efficiency;

- objectives are not clearly defined and are very broad;

- the unit is composed of number of people with limited contracts (CDD).

Recommendations

- there is a need to strengthen basic science in particular in immunology;

- objectives need to be better defined with a limited number of topics and a short list in pathogens to be studied.

3 • Detailed assessments

• UMR 5236 / CPBS

Assessment of scientific quality and outputs

The unit has performed excellent quality fundamental research in the field of virology, bacteriology and anti-infectious pharmacology. Scientific highlights on HIV concern mainly 1/ late reverse transcription, 2/ the characterization of the mechanisms of budding, packaging, capsid assembly, 3/ the interaction of the matrix with PIP2 lipid and role of the lipids in the assembly, 4/ the antisense transcription, and 5/ the secretion of Tat. In addition, they have made significant contributions on the antiviral role and impact on the immune response of autophagy and the role of autophagy in bystander uninfected cells. The unit has also largely contributed to HTLV research by developing studies on the bZip factor and the Tax protein and the characterization of the endocytic pathway used by Chikungunya virus to infect cells.

The unit is also very active and very well recognized in the field of Brucella pathogenesis, Coxiella host-pathogen interactions and Mycobacterium tuberculosis.

Several teams of the unit have made important contributions in pharmacology such as:

1/ the identification of mutations in the RNA polymerase conferring resistance to the clinical antibiotic lipiarmycin;

2/ innovative strategy to block antibiotic resistance mechanisms;

3/ novel anti-bacterial agents targeting Brucella and M. tuberculosis;

4/ design of inhibitors against enzymes involved in the resistance to anti-cancer treatments.

Several physicians are members of the unit and this association leads to original, mostly fundamental projects.

More than 170 original articles have been published during the period, some in high impact factors journals IF>5 (EMBO J, Blood, Plos Pathog, Journal of Infectious Diseases, Nucleic Acid Research), and >10 (J Cell Biol, Autophagy) of which 106 are signed with members of the CPBS as main contributors. Several book chapters and reviews have been also published.

Assessment of the unit's academic reputation and appeal

The unit has a very good academic reputation. The CPBS has strong local, national and international (Europe, USA, Canada, Japan, Australia, South Africa) collaborations and contributes to international scientific collaboration programs. Teams of the unit participate to scientific networks (CFATG, ANR ChikVendom, KerArbo, Modyca consortia, institute of computational biology…). Some members have set up the national network on therapeutic targets against brucellosis and tuberculosis. One team participates to the Labex EpiGenMed. The unit has been involved in the Franco-Chinese scientific cooperation on infectious disease.

Members organized or co-organized several national meetings or symposia (Montpellier infectious diseases meeting, national RNA meeting, French biophysical society…). They are regularly invited as speakers in national and international conferences. They are members of several advisory committees (CoNRS, Université Montpellier), scientific societies, scientific councils (ENS, CPBS, INSB), and of the management board of the Faculty of medicine of Montpellier. Some are members of journal editorial boards. Many of them performed expert services for several international journals, national and international grant applications (ANRS, ANR, FNRS in Belgium).

CPBS members regularly participate in juries for PhD fellowship attribution, PhD examination, HDR board in Montpellier or elsewhere in France.

During the last 2 years, there has been a significant staff increase from 41 to 49 permanent positions and 18 to 27 staff under contract (postdoctoral fellows, PhD). During the period, 6 CPBS scientists have obtained a permanent position: 3 at the CNRS, 1 MCU at the Université Montpellier, UM1 and 2 at INSERM showing that the unit has been very active and successful to promote young researchers and in hiring staff scientists. Several members of the unit have received awards (young researcher Sidaction, FRM, Fondation Del Duca Price) or « Primes d'excellence scientifique ».

The unit has been successful in obtaining grants from national and international funders such as CNRS, Infectiopôle Sud, Sanofi through the Aviesan alliance, FRM, INCA, ERASMUS AVERROS international program, Marie Curie European grant, ANR, ERA-NET, FACCTS, ANRS, Sidaction, Federal institute in Germany, Deinove. In fact, the unit has attracted several new researchers (CR or DR CNRS) or engineers (CNRS) and assistant engineers. A new team has joined in 2011 (ATIP/Avenir). The Unit has hosted a numbers of students (masters, PhD, BTS), 17 postdoctoral fellows, and associated professors including from international countries (China, Ireland, Spain).

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

The CPBS is highly involved in the local environment. The unit participates to the Montpellier Infectious Diseases (MID) consortium, the Bio Santé Rabelais pole and the University Hospital Institute (IHU) on infectious diseases. The CPBS is an important player in infectious disease research in the Languedoc Roussillon region which is one of the research priorities locally.

Several members of the unit have research programs with technology companies such as DEINOVE. The unit created and hosted Deinolab (joined laboratory between DEINOVE and CNRS). They are authors of about ten patents.

The unit participated in « le salon de l'enseignement supérieur ». They cooperated with the MGB pharma. They are members of the directory board of the Department of Biology and Health Council and are thereby involved in decisions regarding biological science at the Université Montpellier. They provide expertise on health risks and provide scientific expert reports dedicated to decision makers of public authorities. They participate in the CNRS training program "Formation d'entreprises" and in the organization of « la fête de la science » They provide courses for high school students.

The unit has been involved in the establishment and activities of the regional network for BSL3.

Assessment of the unit's organisation and life

The CPBS unit (about 76 people: 49 permanent and 27 under contract) is divided in 10 teams lead by a team leader except for team DTI lead by 2 leaders.

They have access to shared services on the CNRS campus (technical service, computer service, communication, website). The support service meets once a month to discuss administrative and financial issues. They shared these facilities with the two neighbouring institutes (CRBM and IGMM). The animal facilities (A3) are on the campus of the Université Montpellier and I3 insectaria are planned to be installed at the IRD. During the visit, the technical staff raised the problem of governance for the people working for the shared services and the accessibility of the INSERM staff (n=1) to the formation programs. The position of the CEMIPAI platform within the CPBS is not clear to the experts committee.

When funding is available, students and postdoctoral fellows have the opportunity to participate in international meetings. The scientific animation is achieved by weekly external or internal seminars. In 2011 and 2012, the "journées du CPBS" were organized outside the campus to present and exchange scientific results of the different teams and to discuss the future directions of the CPBS. Some of the teams interact, but the inter-team scientific collaborations should be strengthened.

Assessment of the unit's involvement in training through research

The CPBS is affiliated to the CNRS and to the Universités Montpellier 1 and 2 (UM1 and UM2). Its members have participated in policy decisions, teaching activities and research training of students. The CPBS belongs to the Doctoral School CBS2 (Sciences chimiques et Biologiques pour la santé) of Montpellier Universities. During the visit, the new director of the Doctoral School attested that the unit is very active in training PhD students and the unit is very successful in finding money for students. He also mentioned that the Languedoc Roussillon region does not provide PhD funding for the laboratories.

There is no specific teaching at the Doctoral School but unit members participate in the training of PhD students from 4 PhD schools and from 7 masters in Montpellier, Lyon, Antilles Guyane and Italy. Several members of the unit are involved in scientific councils of Montpellier Universities.

32 phD students have been trained during the evaluated period in addition to students from masters degrees, faculty of medicine and pharmacy, engineer schools and institutes of technology. 19 PhD and 2 HDR have been defended.

Members of the CPBS are involved in the co-organization of EMBO practical courses, courses at the École Pratique des Hautes Études.

One of the members is the project manager of the master ERASMUS MUNDUS EDAMUS.

Assessment of the five-year plan and strategy

All the CPBS teams will join the new CRIC structure with some re-organization (See common project below).

• INSERM U1058

Assessment of scientific quality and outputs

The unit is dedicated to translational research on infectious diseases and international health with a multidisciplinary approach. Three topics are developed in particular:

1) transmission and prevention of the HIV infection;

2) interaction between HIV and other infectious agents, including Mycobacteria;

3) viruses with mucocutaneous tropism.

The scientific quality of the unit is excellent and internationally recognized. Major achievements are their crucial role in clinical trials to prevent mother to child transmission through breastfeeding or to treat infected infants, mainly in the southern hemisphere.

In terms of fundamental research, they have made important contributions in the understanding of the mechanisms of HIV-1 transmission by breastfeeding and the characterization of the HIV reservoir in the genital compartment

They have a number of projects in limited-resource countries in Sub-Saharan Africa and Asia.

During the period of evaluation (2008-2013), the unit published a very high number of papers with 230 original articles in international journals (138 since 2011) including 33 new publications since september 2013, out of which 105 have been made as main contributors and related to the unit topics. Some of the publications are in impact factor journals >5: AIDS, Clin Infect Dis, Lancet, Lancet Infect Dis, Retrovirology, BMJ, J infect Dis.

Several members (mostly the director) of the unit have been invited to national or international conferences.

Members of the unit are authors of more than 152 abstracts in international conferences and 52 in national conferences (41 related to unit research topics).

The projects of the unit are funded by EDCTP, ANRS, INSERM/DHOS, European Commission (FP7, INCO-DEV), NIDA/NIH, CDC, NIH of which the principal investigator and coordinator of the project is often a member of the unit. Ten research projects were active in 2013.

Assessment of the unit's academic reputation and appeal

The academic reputation and appeal of the unit is outstanding.

The unit has a very large network of regional, national and international (Europe, Africa, Asia, USA) collaborations with a very active partnership in particular with developing countries.

Several illustrating examples are listed:

- together with the University of Bergen, the INSERM unit 1058/Université Montpellier is coordinating the PROMISE Network. The objective of this scientific network is to encourage research on infant nutrition, paediatric infectiology and transmission of infectious agents by breastfeeding;

- the unit 1058 is an active member of the HARP (HPV in Africa Research Partnership) network of academic institutions aiming to provide rigorous evidence to guide cervical cancer screening programs for women living with HIV in Africa;

- the MONOD Network dedicated to the improvement of pediatric HIV care in developing countries;

- the INSERM unit 1058 is a founder member of the Labex EpiGenMed (with 39 research units/teams from the Montpellier region). One postdoctoral position will be recruited in 2014.

The head of the unit is regularly requested for expertise (EDCTP stakeholders meeting, advisor for research laboratory, NIH-NIAID investigator-initiated program project application…).

Members of the unit are reviewers for scientific journals.

Since 2011, 17 people joined the unit including 3 university staff, 2 postdoctoral fellows, 1 hospital MD (PH), 3 study engineers, 1 communication officer and 7 international PhD students. Two foreign researchers with a sabbatical year, have joined in 2011 from Bergen University, Norway and in 2012 from Laval University, Quebec.

One member of the unit went for a 12 months mobility period in Ho Chi Minh City (Vietnam) on a program on TB and mycobacteria at the Pham Ngoc Thach hospital.

The unit has been approached by the TransDiag team from the EFS (Établissement Français du Sang/French Blood Service, member of the AVIESAN Coalition) and by a CNRS team to join the unit for the next five-year research contract. This project would be completed by merging the unit with UMR 5236 in order to create the research center on chronic infections under the direction of Mr Philippe VAN DE PERRE. Together, the scientific activities of the unit are extremely attractive for new people and new teams to join.

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

The unit develops innovative translational research projects in the context of a strong regional, national and international partnership. Their activities are perfectly integrated in the strategy plans of the région Languedoc Roussillon for infectious disease research recognized by the « pôle biologie-santé François Rabelais ».

The unit has also a very strong partnership with the CHRU Montpellier. The director is the vice president (in charge of research) of the CHRU Montpellier Directorate and member of the scientific committee, Faculty of Medicine, Université Montpellier 1. He is highly successful in promoting clinical research in Montpellier and gave a revolutionary impulse to this research, as testified by the hospital general director during the visit of the experts committee.

Members of the unit have created the start-up OMUNIS (development, commercialization of innovative tools for diagnosis for chronic infectious diseases) with the support of the region. They hold 5 patents since 2011 (9 since 2008).

The unit is also very good in disseminating their research to the general public. They participated in a press conference in 2013 for the release of the preliminary data of the ANRS 12174 clinical trial (infant PreP to prevent breast milk HIV-1 transmission) that was widely covered in the media. They participate in programs to promote public understanding of science, such as La Recherche, the INSERM magazine « Science et Santé ». They have also been involved in a film on the dynamism of health research at the Université Montpellier, in the HIV/AIDS 1st december day's animation.

Assessment of the unit's organisation and life

The unit is actually composed of about 40 people (28 at the beginning in 2011).

The unit does not have its own heavy equipment but benefits from the access of technologic platforms around.

During the visit of the experts committee, the ITA staff expressed their concerns about the future of the high numbers of people under CDD. When funding are available, students and postdoctoral fellows have the opportunity to participate to international meetings. Scientific meetings of the unit as well as working group meetings are frequent. Since more than one year, several joint meetings have been organized with the CPBS and TransDiag.

Assessment of the unit's involvement in training through research

The INSERM U 1058 belongs to the Doctoral School CBS2 (UM1 and UM2). Several members of the unit are teaching. The director coordinates 2 modules “from infectious agents to hosts” and “bacterial and viral pathologies, retrovirology and transposons” at the university. Since 2011, 13 new PhD students, several masters 2 and each summer, about 10 masters 1 have joined the unit. 7 students have defended their PhD.

During the visit of the experts committee, the new director of the Doctoral School attested that the unit is very active to train PhD students. The unit is very supportive to the students in obtaining funding and the fact that the academic reputation is excellent favours funding. For example, they have access to co-funding by the MD/PhD training program between the university and the Hospital. Furthermore, the unit is very active in training and teaching people in developing countries. Some members participate each year in an international university diploma on HIV care at the University of Ouagadougou in Burkina Faso.

Members of the unit participate in distance learning program or guide on infectious diseases, at the Université des jeunes chercheurs (Sidaction).

Assessment of the five-year plan and strategy - Common project: CRIC

All the members of the unit will integrate new teams DTI and TCCI of the new CRIC structure. See common project below.

The new UMR structure, CRIC (Research Center on Chronic infections) as a provisional name, will combine the UMR 5236, the INSERM unit 1058, the TransDiag team and a MPNTT team (actually in the UMR 5235, DIMNP: Dynamique des Interactions Membranaires Normales et Pathologiques, dir: Ms Catherine BRAUN-BRETON). The structure will be located in the CPBS/CNRS building Route de Mende except Team DTI which will be located in the university teaching hospital (CHRU) until 2017 and then in a new Hospital Laboratories building currently under construction. Together about 140 people will participate in the center in January 2015. Several other teams might join in the future. Since July 2012, there have been several meetings between the team leaders to discuss the organization of the center. The staff laboratories have also participated in some of the discussions. The director of the CRIC will be Mr Philippe VAN DE PERRE, the previous INSERM U 1058 director and the vice director, Mr Jean-Michel MESNARD belonging to the previous CPBS. The director and vice-director were elected by a consensus. To facilitate the transition between the former direction team and the new one, the direction teams of CPBS and INSERM U1058 will work together in 2014.

At the beginning, the center will be divided into eleven teams coordinated each by one or two researchers with three main axes:

1/ Host pathogen interactions at molecular level;

2/ Host pathogen interactions at cellular level;

3/ Host pathogen interactions at the level of the patient.

Each team of the UMR 5236 will continue except former teams 4 and 6 which decided to fuse into the new team BERA and former team E7 which will join the new team TCCI. The people of the INSERM U1058 will be in new teams DTI, TCCI or MPNTT, TransDiag team will be in DTI and the CNRS team will have its own team MPNTT. The technological platforms CEMIPAI and BIOCAMPUS and the CHRU Montpellier will be strong partners of the center.

However the position of the CEMIPAI platform (located in the CPBS/CNRS building) within the center was not clear to the experts committee.

The center will benefit from the common services of the CNRS center and the closed local scientific environment of the 2 other centers in the same building (CPBM and IGMM). We are extremely satisfied by the commitment and appreciations of the potential management bodies and have great hopes in the involvement of CNRS (principal management body), NUM (Nouvelle Université de Montpellier), INSERM and EFS as “co-tutelles” with a strong collaboration agreement with CHRU Montpellier.

The 3 thematic axes will not be departments but rather spaces for scientific animation coordinated each by an opinion leader to promote exchanges, animation, new thinking.

There will be an administration and management team with a general secretary. This team will include a grant office with a lab manager that has been recently recruited by the INSERM. 10 % of the funding obtained for each project will be dedicated to building inter-team solidarity.

The common main goals of the center are:

1) to improve care and prevention of chronic infections by combining basic science, translational and clinical research;

2) to study host-pathogen interactions at the molecular, cellular and patient levels;

3) to facilitate innovation and industrial partnerships;

4) to establish the place of chronic infections and their control in national and international programs.

This new structure represents a unique opportunity to develop translational research projects in collaboration with clinicians and basic researchers for improving the prevention of the infectious risks. The different teams have complementary expertise, with a high potential to perform outstanding research. The 3 axes are totally integrated in the « pôle Rabelais » scientific strategies.

The fusion of the different teams will greatly increase the visibility of the infectious disease research locally, in France and internationally. This should help to launch ambitious, comprehensive calls for projects (Horizon 2020, NIH, EDCTP-2…). This new center will have the potential to attract new teams and excellent researchers. It also represents a first step to federate infectious disease research in the région Languedoc Roussillon.

The research activities of the center should not overlap with the one of the 2 other centers in the same building, CRBM and the IGMM. Some teams have already some collaborations and this should be highly encouraged.

During the visit, the experts committee met the managing bodies from the Université Montpellier, the CHRU and the EFS. They were all very supportive and very enthusiastic about the creation of the center and the fusion of the different entities. The general director of the CHRU confirmed that the themes of the future center are institutional priorities with very strong translational aspects. Twenty people are clinical academics (HU) in the new center. One MD/PhD training fellowship has been already allocated for the INSERM U 1058. The CHRU director attested that the CRIC director has really given a revolutionary impulse to the translational research in the region. The president of the university also confirmed his strong support, illustrated by the fact that they have already provided financial support to the CPBS and the INSERM U 1058 in the past for lab functioning, one postdoctoral position and scientific meeting organization. One MCU position and one research engineer position have been allocated to the CPBS these last 2 years and another position will be allocated in 2014 to the U 1058 INSERM unit. Several chairs of excellence will potentially be opened for the Labex EpiGenMed in parallel with the CHRU. The director of the EFS also affirmed his strong support for the project. He said that the fusion of TransDiag with the future DTI will be crucial to improve blood safety in particular in emerging countries. It will be a tremendous opportunity to give an international dimension to TransDiag and the link with the industry will be reinforced by this fusion.

The INSERM and CNRS representatives will wait for the AERES experts committee conclusions before giving their opinion about the center, but are quite positive since each of them were supportive of the previous entities (CPBS for CNRS and unit 1058 for INSERM). The INSERM representative specified that they already provided a manager position. The CNRS representative specified that the platform CEMIPAI should be separated from the center.

The meeting with the new director of the Doctoral School CBS2 was also very positive. The different entities are very active in training and in finding money for their students. The different teams are attractive for the students. There is 6 MERT grants ongoing for PhD out of 20 delivered/year for all the Doctoral School. The fusion of the different entities should be an added value for the attractiveness. There is no specific teaching at this Doctoral School but several members are teaching elsewhere, for example in masters or coordinate masters courses. Some participate in Erasmus programs. There is also the opportunity to get some fellowships from the « Infectiopôle Sud ». The Doctoral School uses also the different platforms of the future CRIC for training. The follow up of the students after their training in the different entities is not very easy since many are foreigners. However amongst those who have been followed 5 years after their PhD, 20 % have an academic carrier and 50 % are doing a postdoctoral period.

Strengths and opportunities

- the creation of the center will bring complementary expertise from basic scientists to translational scientists together with clinicians;

- already, interactions with technology transfer companies have started;

- the new center has a very strong support from the Hospital, the university and the EFS;

- the creation of the center will be a major development for the région and France;

- the thematics are totally integrated in the « pôle Rabelais » scientific strategies;

- this represents a high potential to attract new teams and excellent researchers and also a first step to federate infectious disease research in the Languedoc Roussillon region;

- the fusion of the different teams will greatly increase the visibility of the Montpellier infectious disease research locally, in France and internationally;

- the fusion should increase the potential to apply to international organizations for funding;

- the CRIC will have access to common services and technical platforms;

- the new center will benefit from the excellent scientific environment with the 2 other centers in the same building (CPBM and IGMM);

- the entire staff is very enthusiastic about the fusion, there is a lot of hope and a collective adhesion to the project.

Weaknesses and threats

- the experts committee has noticed that there is not enough collaboration between the teams within the center;

- the future director will have to invest a fair amount of his time in the organization of the future center;

- the organization of the governance is not clear and this has been obvious regarding the policies of allocation of space, of new recruitments, of scientific strategy, of budget allocation, of answers to calls for funding. Moreover the decision-taking process is not clear, although a consensus from all team leaders is planned to be obtained before taking strategic decisions. The governance of the future center should be clearly identified and planned long in advance. Rules should be well defined and communicated to the staff:

- a number of staff are under short-term contracts;

- the position of the CEMIPAI platform within the center is not clear.

Recommendations

- the governance should be guided by establishing an international Scientific Advisory Board, which meets annually, to provide feedback and advice on scientific strategy and governance of the center (CRIC) as for example creation of new teams and recruitment of new group leaders;

- the managing team has to formulate a clear view of how the work of the CRIC is distinct from that of similar units both in France and overseas, and to articulate this view both to members of the CRIC and, via the website and other means, to the outside world. This is not a mission statement, but a more substantial, succinct and specific summary of the unique identity of the center;

- An annual symposium has to be held, including a few overseas speakers, to raise the profile of the CRIC nationally and internationally;

- the visibility should be improved by improving the website very significantly (in particular the English version);

- the center will benefit from increasing internal collaborations;

- the position of the CEMIPAI platform has to be clarified in term of projects, funding and personal;

- the recruitment of an immunology team would be an added value in the future;

- the managing team has to consider introducing a system of mentorship, in which an experienced member of staff agrees to meet a more junior member (e.g. annually) to provide informal advice on scientific strategy, career progression etc. In this voluntary system, the mentor should be outside the mentee's group: in particular, the mentor should not be the line manager of the mentee.

4 • Team-by-team analysis

Team 1: Metabolism of retroviral RNA (MRR)

Name of team leader: Ms Marylène MOUGEL

Workforce

Team workforce	Number as at 30/06/2013	Number of 01/01/15
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	2
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**5**	**5**

Team workforce	Number at 30/06/2013	Number at 01/01/2015
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	3

• Detailed assessments

Assessment of scientific quality and outputs

The team leader is a retrovirologist with a DR position at CNRS and is affiliated to the CPBS since its opening with more than twenty years experience in studying retroviral RNA. These 10 last years, the team has focused its attention to the retroviral RNA in a cellular context, and therefore has developed new tools, especially using fluorescence microscopy in order to follow retroviral RNA dimerization and packaging during assembly of viral particles and subsequent DNA synthesis produced by reverse transcription.

In the period 2008-2013, team MRR obtained a quite significant level of publications (15), out of which 11 publications were signed as first author and 6 as last author. Nucleic Acids Research, RNA Biology and Retrovirology are the most relevant journals that published the work of team MRR. One paper is actually under revision in Plos Pathogens. Team MRR is co-author of a review published in Nature Cell Biology in 2011.

Assessment of the unit's academic reputation and appeal

The team MRR has been quite active since 2008 with the obtaining of two permanent positions (1 CNRS researcher who left for Pasteur Institute - 1 assistant professor of Université Montpellier), the defence of two PhD thesis plus one close to the end, the recruitment of three post-doctoral fellows (from China, Spain and Ireland), the obtaining of grants from ANRS and recently from EC-IEF Marie Curie action. Team MRR has also a large number of partners in Montpellier, in France, in EU and in US.

The team leader is quite active at the SFFBM and its RNA section, and also as an ANR expert, a journal reviewer or a tribunal member for numerous PhD thesis. Its social networking is growing and publications of team MRR are always in partnership with local, French or international teams.

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

New studies on a promising antiviral compound are expected to favour future interactions with biopharma industry.

One MMR team member is engaged in infectious disease surveillance within a little city close to Montpellier.

Assessment of the unit's organisation and life

The team MRR is composed of one DR CNRS, one MCU and one AI (Université Montpellier) plus one post-doctoral fellow IEF-Marie Curie (2013-2015), one post-doctoral fellow ANRS (2012-2014) and one PhD student (last year).

Assessment of the unit's involvement in training through research

Defense of two PhD thesis has been performed. One is close to the end. Numerous Master students have been hosted .

Assessment of the five-year plan and strategy

Still focused on the viral RNA, team MRR's visible challenge is to unravel the detailed molecular mechanisms directing the retroviral RNA packaging and the intra-viral control of reverse transcription. The recent incorporation of a highly experienced post-doctoral fellow supported by an IEF-Marie Curie action also allows team MRR to extend its research to two other highly relevant topics. Therefore projects of team MRR are organized around four main questions which are:

1/ the spatiotemporal relationships from HIV and MLV RNA nuclear export to particle assembly by the way of intracellular trafficking;

2/ the nucleocapsid-related limitation of reverse transcription in HIV viral particles (an original work developed by team MRR);

3/ the pre-integrative viral trafficking and its transactions with nuclear envelope and MAPK-associated phosphorylation with a comparative study between HIV and MLV to be done;

4/ the characterization of a new antiviral compound that provokes apoptosis of HIV-infected cells (pending confirmation of supporting grant by B & M Gates foundation – Grand Challenge).

Conclusion

- **Strengths and opportunities:**

The spatiotemporal coordination of HIV particles from production to infection is a hot topic with team members as ones of the leaders. Team MRR goals are planned here in a collaborative approach with renown experts. Incorporation of a new expertise relied on the post-doctoral fellow supported by an IEF-Marie Curie action will allow to better tackle experimental approaches at the cellular level, to engage new promising research projects and to develop more partnership with the other teams of the center.

- **Weaknesses and threats:**

The precariousness of the post-doctoral fellow acting as a research leader may provoke a strong pressure in case his projects do not succeed quite fast.

One post-doctoral fellow and one PhD student are close to end their stay. Team MRR is looking how to get supports for new PhD students and post-doctoral positions.

- **Recommendations**

Securing position of the post-doctoral fellow supported by an IEF-Marie Curie action would reinforce team MRR within the CPBS, his “antiviral project” will provide the financial support, in particular if he get the confirmation of funding from the B & M Gates foundation (Grand Challenge). The expected success will favour a positive projection in a mid-term perspective.

The needs to get more grants and to engage post-doctoral fellows and PhD students are an absolute requirement for team MRR to ensure the success to their research projects.

More interactions within the center should also be convenient to strengthen team MRR positioning within the global project proposed for the center for the next five years.

Team 2: Membrane Domains and Virus Assembly (MDVA)

Name of team leader: Ms Delphine MURIAUX and Mr Cyril FAVARD

Workforce

Team workforce	Number as at 30/06/2013	Number of 01/01/15
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	3
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		1
N6: Other contractual staff (without research duties)		1
TOTAL N1 to N6	**3**	**6**

Team workforce	Number at 30/06/2013	Number at 01/01/2015
Doctoral students	3	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	2	2

- ## Detailed assessments

Assessment of scientific quality and outputs

One of the team leaders with a virologist background and a CNRS CR1 position, has moved in 2012 from the ENS in Lyon to the CPBS in Montpellier to join the other team leader with an IR1 CNRS who comes from the Fresnel Institute in Marseille. The new team MDVA brings together the expertise in retrovirology and cell biology with the one in lipid dynamics and biophotonics. This association should favour interdisciplinary projects in an expending field recognized nowadays as very fertile (and also very competitive).

In the period 2008-2011, the virologist PI has regularly produced papers in collaboration and a couple of papers as senior author (in Retrovirology and J Virol). The biophysist PI has also been associated to several papers and contributed two papers as first author in Biophys J, including one in 2014. The scientific production of the recently created team has not yet been translated in publications but this of course will require more time. 3 papers are currently submitted. One review in Virus research is signed by both team leaders.

Assessment of the unit's academic reputation and appeal

Both team leaders have established a network of international and national interactions. They participate to scientific national meetings, have organized a few of them, and attend the important meetings worldwide. They have 2 PhD candidates who are currently applying for fellowships to join the team. In addition, two candidates are applying for CR CNRS or INSERM position to be recruited in their team. They also belong to several scientific councils (GDR Microscopie du Vivant; scientific/organizing committee of the International Retroviral Nucleocapsid Symposium, PLATIM and Doctoral School BMIC at the ENS Lyon, CPBS, MRI…). The team MDVA recently obtained an ANR grant on their project about the transactions between viruses and cellular membranes.

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

Participation to “Fête de la Science” and related social events to present science to non-scientists. One of the team leader is also consultant for “Aquacouleur” and “Bertin technologies”.

Assessment of the unit's organisation and life

The team is actually composed of 1 CR1, 1 IR1 and 1 ITA, plus 3 PhD students.

Assessment of the unit's involvement in training through research

Both PI are active in teaching and formation, are experts for student juries and grant evaluations as well as reviewers for international journals. One PhD thesis was defended and the team MDVA currently hosts three PhD students. Two new students have applied to fellowship to join the team at the end of 2014. They also train master students in Biophysics and in Virology.

Assessment of the five-year plan and strategy

Despite a document clearly not well organized and written too fast, the project presented during the oral presentation appears appealing. Focusing on the interplay between viral proteins and host-cell lipids, the team MDVA aims at deciphering the molecular mechanisms underlying the retroviral assembly process. Their projects are organized around two main questions, which are:

1/ the role of membrane nanodomains in the assembly of HIV and Flu;

2/ the regulation of actin cytoskeleton and membrane curvature during HIV assembly.

The team has established a large body of collaborations at the national and international level. Combining state of the art microscopy (sv-FCS) and high-resolution microscopy (STED, PALM…), the team plans to analyse the dynamics of Gag and PiP2 in Jurkat T cells. They also develop alternative models such as GUV (Giant Unilamellar Vesicles). The team is developing projects at the interface with biophysic including the study of HIV assembly at the single particle level using atomic force microscopy. They recently applied their knowledge and approaches to the study of influenza viruses.

Conclusion

- **Strengths and opportunities:**

The complementarity of the two team leaders represents clearly an advantage. The field is competitive but of great interest. The team leaders are well connected to important scientists of the field. The development of the Flu project represents, in addition to its obvious scientific interest, an opening to non HIV sources of funding (which are predicted to be subjected to important cuts). They recently obtained an ANR grant which will help them to secure the salary of a technician.

- **Weaknesses and threats:**

The team is very recent and has yet to get accepted by the community as specialists of the lipid dynamics in the field of HIV assembly. They are not yet fully integrated and do not have yet joint projects within the new center.

- **Recommendations:**

The experts committee encourages the team MDVA to go on their research at the interface between cell biology, virology and biophysics and to aim at addressing important and ambitious biological questions. Considering the highly competitive field of HIV, the team must be reinforced by recruitment of talented students, since the ongoing PhD will defend thesis at the end of 2014. Support from the center (with scientific technician) could also be important to strengthen the team.

Given that the team is headed by two team leaders, it is recommended to have special attention about the management of the team to secure a productive environment for the team members.

The team MDVA may need to put some efforts for their integration in their relatively new scientific environment, at the level of the new center and with other neighbouring units which host numerous cell biologists.

Team 3: Bacterial enzymes and resistance to antibiotics (BERA)

Name of team leader: Ms Corinne LIONNE and Mr Konstantin BRODOLIN

Workforce

Team workforce	Number as at 30/06/2013	Number of 01/01/15
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	3	3
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	2
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**6**	**7**

Team workforce	Number at 30/06/2013	Number at 01/01/2015
Doctoral students	2	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	6	
Number of Research Supervisor Qualifications (HDR) taken	3	
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs

The team BERA proposed for the 2015-2019 period combines the expertise of two former teams of CPBS: (i) the team of Mr Konstantin BRODOLIN whose main interest was transcription and antibiotic resistance, and (ii) the team of Ms Corinne LIONNE that was dealing with enzyme and aminoglycoside resistance, which after the last evaluation by AERES, was invited by the CNRS to modify its research activity in order to better fit with the unit's research priorities. This has been done by focusing on bacterial resistance to aminoglycosides, a change which was acknowledged in a mid-term evaluation report by the CNRS in December 2012.

The former activity of the team was partly dealing with the study of nucleoside analogues used as antiretroviral drugs. In particular, the team was interested in understanding the phosphorylation events required for activating such molecules using various approaches, including 1/ transient kinetics study, 2/ molecular docking, and 3/ in silico simulations. Since 2011, the team is interested in understanding how aminoglycosides are inactivated by phosphotransferases (APH) in bacteria, using its own expertise in enzymology, structural biology, molecular docking and virtual screening, medical chemistry and microbiology. The team has already identified several APH inhibitors that could be used to restore bacterial sensitivity to aminoglycosides, which are currently under investigation. Importantly, this recent thematic switch already led to one publication (FEBS Lett 2012, where the team leader appears as senior author).

The other theme of the team is hold by the second team leader who joined the CPBS in 2008. Using a combination of genetic, biochemical and structural approaches several aspects of bacterial transcription including the molecular mechanisms of antibiotics targeting the RNAP have been studied. This led to the identification of the novel mechanism of action of a newly introduced antibiotic (Lipiarmycin) and to a publication in EMBO J (2010). The team has developed several expression systems (e.g. random promoters library, vector for the expression of all subunits of M. tuberculosis RNAP) and a fruitful collaboration with a private company (DEINOVE) that will allow screening for antibacterial agents.

During the 2008-2013 period, the team has published about 42 articles (of which 40 % have been signed as main contributors), including five articles in the excellent journals EMBO J (2010) or Nucleic Acids Res (2008, 2012), and several articles in very good specialty journals as first or last authors (e.g. Chem Biol 2009, J Allergy Clin Immunol 2008, Int J Antimicrobial 2010 & 2009, J Mol Biol 2011, PLoS Comput Biol 2011, FEBS Lett 2012, Biochem Pharmacol 2013, Biochemistry 2008 & 2009).

Assessment of the unit's academic reputation and appeal

The team is embedded in several but mostly national networks. One of the team leaders co-organized 3 national congresses, a French–Russian seminar in Montpellier and is member of the executive board of the SFB (French Biophysical Society) and member of the SFBBM (French Biochemistry and Molecular Biology Society). The other team leader gave oral presentations at three international meetings (FASEB, 25th RNA Pol. Workshop). The fund raising activity from national or regional source is very good, with several grants from ANRS, INCa, ANR and a postdoctoral fellowship from the Infectiopôle Sud Foundation. International networking is starting with UK based scientists.

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

The team is very strongly involved in industrial research development and more than half of the team’s budget comes from contracts involving the private company DEINOVE. The project DEINOl (bioethanol) was granted 160 k€ for three years and the project DEINOBIOTIC (antibacterial molecules) received a budget of 350 k€ for four years. In addition a collaboration between the CNRS and DEINOVE resulted in the creation of an investigation laboratory DEINOLAB (255 k€/3 years) that was hosted by the team until 2010 with the creation of 32 full time jobs. Four patents have been obtained among which three with CNRS and DEINOVE as inventors and one patent application is currently submitted.

Assessment of the unit's organisation and life

The group is composed of 3 senior scientists (1 CR INSERM, 2 CR CNRS), 2 engineer and technician, 2 post-doctoral fellows, 3 PhD students. There is no clear indication about the way the team is organized and functions on a weekly basis.

Assessment of the unit's involvement in training through research

During the evaluation period, 2 PhD thesis were defended (with between 1 to 3 publications/student) and 4 post-doctoral fellows were hosted and recently two postdoctoral fellows and one PhD student were recruited. Two PhD students are currently trained. One of the team leaders co-organized three EMBO practical courses on transient kinetics for the study of biological macromolecules and delivered lectures at EPHP, at the Master level, in 2011.

Assessment of the strategy and the five-year plan

For the coming period, the team BERA will develop two main projects, based on the team leaders' expertise which are:

1/ understanding aminoglycoside modifying enzymes in bacteria, with a focus on the role of APH, and development of inhibitors of such enzymes in order to restore bacterial sensitivity to aminoglycosides, and

2/ understanding bacterial resistance to antibiotics targeting RNA polymerase, in particular in E. coli and M. tuberculosis, in order to propose novel drugs.

While the expertise of the two team leaders has to be acknowledged, it appears that they are both planning to continue independent researches in very competitive areas. They should have taken the opportunity of the creation of a new team to build up a really common project. This would contribute to increase the critical mass and the international visibility of the team. A unique leader would also facilitate the future management of the team.

Conclusion

- **Strengths and opportunities:**

The former recommendations made by AERES and CNRS have been carefully taken into account, and successfully followed. The new project has already granted one publication. The fusion between the two teams, and interactions of the new team with other teams at CRIC will likely be fruitful through expertise sharing and synergy. The two team leaders have a few very good publications in their field (NAR, EMBO J), which should help them embarking in novel and wider collaborative networks. The proximity of the CEMIPAI platform will be of great help in the context of the forecasted researches.

- **Weaknesses and threats:**

The field of antibiotic resistance is very competitive, and to date, the team is mostly involved in national collaborations with low international visibility.

There is no common project between the two team leaders.

The dual direction of the team might be a source of problems in the future in term of management.

- **Recommendations:**

The team leaders should be more aggressive at promoting their research and increasing their visibility at large and prestigious international conferences. The team leaders should broaden the portfolio of potential international collaborators. The team should join large international networks on antibiotics resistance. More translational research should be developed in addition to basic discovery in the field of APH inhibitors and resistance to RNA polymerase inhibitors.

The two team leaders must build up at least one common project.

One of the team leaders should consider taking the lead in the future to improve management.

Team 4 : Mycobacterial pathogenesis and novel therapeutic targets (MPNTT)

Name of team leader: Mr Laurent KREMER

Workforce

Team workforce	Number as at 30/06/2013	Number of 01/01/15
N1: Permanent professors and similar positions		1
N2: Permanent EPST or EPIC researchers and similar positions		1
N3: Other permanent staff (without research duties)		1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6		**3**

Team workforce	Number at 30/06/2013	Number at 01/01/2015
Doctoral students	5	
Theses defended		
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	1	2

• Detailed assessments

Assessment of scientific quality and outputs

This is a new team. The research goals of the team deal with various aspects of mycobacterial pathogenicity and therapeutic development to combat mycobacterial infections. This includes:

1/ the study of serine/threonine kinase-mediated regulatory mechanisms involved in cell wall biosynthesis and the study of the mode of action and discovery of various drugs targeting the mycobacterial envelope with a strong focus on mycolic acids synthesis;

2/ the molecular dissection of pathways involved in the synthesis of other components of the mycobacterial envelope (e.g. LOS);

3/ the implementation and exploitation of novel alternative cellular and animal models (in this case, amoebas and the zebra fish) to study mycobacterial pathogenicity using two mycobacterial species, Mycobacterium marinum and M. abscessus.

During the 2008-2013/early 2014 period, the team leader has published about 50 primary articles, including 1 recent PNAS, about 10 articles in excellent specialty journals (mostly J Biol Chem and Mol Microbiol) as senior author and 1 article in Nature Chemical Biology as second to last authors, 5 review articles and book chapters, 1 patent, as well as many other articles as co-authors, which reflects an intense and fruitful networking activity. Of note, the recent development of novel cellular and animal models of mycobacterial pathogenicity already granted an important publication in Mol Microbiol in 2011 and a recent publication in PNAS (in press) where the PI appears as last author.

Assessment of the unit's academic reputation and appeal

The team leader has a very good (international and local) visibility in the field of mycobacterial molecular pathogenicity, as attested for instance by the high citation index (56) of one of his recent reviews (Mol Microbiol, 2010), several invitations to give seminars in various institutes, and as a speaker in national and international conferences and meetings (e.g. 8th International Conference on the Pathogenesis of Mycobacterial Infections, Stockholm 2011; EMBO Conference on TB 2012), participation to the EpiGenMed laboratory of excellence (LabEx), and participation to several PhD committees.

The team leader is efficient at networking, on the national and international levels, recruited two permanent scientists (one CNRS senior research associate and one associate professor) and several postdoctoral fellows, and hosted one visiting professor in 2012-2013.

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

The team leader participated to one review in the popular press (Biofutur), has one contract with industry (Biorad), and holds one patent. This is a very good level of interaction with the social, economic and cultural environment.

Assessment of the unit's organisation and life

In January 2015, the group will include 2 senior scientists, 1 technician/engineer (to be recruited), 2 post-doctoral fellows and 5 PhD students. Team meetings are organized weekly to discuss on-going projects and joint meetings with the U1058 unit have started.

The ability to raise funds is excellent, both from private (Bio-Rad) and public entities (e.g. ANR, VLM), and resulted in over 700 K€ raised in the 2008-2013 period.

Assessment of the unit's involvement in training through research

Three PhD students graduated during the 2008-2013 period. Two other PhD students will graduate in 2014. Three MSc students completed and two MSc students are currently completing their Master degree during the 2008-2013 period.

Assessment of the strategy and the five-year plan

For the coming period, the team leader decided to leave UMR 5235 and to join the proposed new Center of Research in Chronic infections (CRIC) in order to enrich basic studies with more translational approaches and to benefit from additional technological facilities such as a dedicated zebrafish facility, imaging facilities, BSL3 laboratories, animal facilities and screening platforms. The team leader has already started a fruitful collaboration with the future director of the CRIC which resulted in a common patent. In the coming period, the team leader will focus his efforts on three research axes, which are:

1/ deciphering the molecular bases of smooth to rough transition in M. abscessus, a mycobacterial species of primary clinical importance, especially in CF patients, using molecular biology and the zebrafish model;

2/ deciphering the role of mycobacterial lipases in mycobacterial pathogenicity;

3/ understanding the mechanisms of mycobacterial resistance to various drugs targeting the cell wall.

The project is ambitious and original with a good balance of low risk and more risky/high reward tasks and is in line with the expertise and previous activity of the team leader. It is supported by several grants, including two recent grants from VLM and ANR co-ordinated by the team leader.

Conclusion

- **Strengths and opportunities:**

The team leader is a clearly recognized expert in his field. The project is ambitious and original with a good balance of low risk and more risky/high reward tasks. The networking and fund raising activities are excellent. The transition from UMR 5235 to CRIC is logical, and no overlap is foreseen with the mycobacterial research that will continue at UMR 5235. New collaborations at CRIC, and involvement of the team in more translational research is a unique opportunity that should be fully exploited.

- **Weaknesses and threats:**

Implementation of the team in the new structure needs to be fully supported, and an appropriate environment and personal support must be provided to the team leader, including technical staff.

- **Recommendations:**

The team leader should be more aggressive at publishing in higher impact journals. More permanent staff should be recruited. One associate professor in epidemiology will join the team. At least one more permanent researcher holding an HDR and with expertise in microbiology and/or host-pathogen interactions has to be attracted in the team as soon as possible.

Team 5: Virus-host interactions (VHI)

Name of team leader: Ms Laurence BRIANT

Workforce

Team workforce	Number as at 30/06/2013	Number of 01/01/15
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		1
N6: Other contractual staff (without research duties)	1	1
TOTAL N1 to N6	**6**	**7**

Team workforce	Number at 30/06/2013	Number at 01/01/2015
Doctoral students	1	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The team leader is a retrovirologist, specialist of host-HIV interactions with a DR position at CNRS. Since 2008, the team is focused on viral capsid assembly (structure and dynamic), and elucidation of its role in viral replication at the interface with host cell proteins. Beside structural basic science, these approaches allowed to characterize cell pathways affected by capsid proteins in favor to viral replication. Indeed, understanding structural and non-structural roles of capsid proteins have lead to the design of new antiviral which is the ultimate goal of the team. This approach has been successful as highlighted by several publications, a patent and industrial collaboration. HIV expertise has been recently and successfully applied to the study of Chikungunya virus (CHIKV).

The team has published an impressive number of papers for a small team of only 3 researchers (23 papers during the period). Moreover, these include specialized journals with high IF such as Retrovirology (8 papers), Plos Pathogens (1 publication), NAR (2 publications) and EMBO (in collaboration). Most of them (13/23) are directly connected to the team work (first and last authors are team members) while the remaining are the results of long term collaboration. 3 supplemental manuscripts have been published since august 2013, notably a NAR paper.

Assessment of the unit's academic reputation and appeal

During the period, the VHI team recruited 3 people and had a promotion highlighting its great academic reputation and appeal.

The team leader served as expert for ANRS, FNRS, and reviewers for FINOVI and ANR. She was also involved in PhD and HDR juries and M2 defences.

The team has built a solid network of local collaborations (with CBS Montpellier and with MIVEGEC Montpellier), inter center collaborations (with teams PPRT, BERA), national collaboration (consortium of chemists at the Université Paris Descartes) and international collaboration (Gavelston, USA).

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

The team had an industrial contract with MGB Pharma based on their work on HIV inhibitors patented.

Assessment of the unit's organisation and life

The team is currently composed of 5 permanent members (one DR2 CNRS, one MCU, one IE Université Montpellier 1, one CR1 CNRS, one technicien TCN CNRS), one assistant engineer (CDD) and 5 students (3 PhD, and 2 M2).

Assessment of the unit's involvement in training through research

With 2 HDR, the team has trained 6 PhD, with 3 still ongoing. In addition, 2 post doc, 1 assistant engineer, 2 IE and several M2 and M1 students have been trained during the period reflecting an important appealing of the team. Intensive involvement in teaching, governance of teaching (ERASMUS program, and board responsibility in “securité sanitaire des aliments) and structuration of life science in Montpellier (One assistant professor has been head of infectiology branch in the pole biosanté Rabelais) participate to their excellent visibility. One assistant professor is actively involved in teaching (elected delegate in the Doctoral School Biosanté, elected at the management board of ERAMUS program, director of BSL3 program, member of CNRS Training program).

Finally they created and still manage an electron microspy platform and a national formation on BSL3 practices.

Assessment of the five-year plan and strategy

As expected from their previous success, the team will follow the same topics and study in parallel HIV and CHIKV capsids both in assembly and cellular traffic. Extending topic to new virus models such as CHIKV is a great move both for funding purpose, as HIV funding is getting more and more competitive, and to apply knowledge to lower studied alphaviruses. Written project was excellent but oral presentation was too dense leading to confusion and questions regarding its feasibility. Briefly the team project is divided in 3 topics, each lead by one senior scientist of the team.

- project 1 on structural capsid assembly, and mode of action-development of drugs targeting the flexible region. This particular topic will benefit from patients samples collected by U1058 team for the drug validation. Two approaches will be developed which are spatio-temporal role of flexible region SP1 in HIV capsid assembly-maturation and RNA structure and analysis of CHIKV capsid structure with both prediction and 3D resolution;

- project 2 deciphering the role of packaged cofactor UNG2 and its influence on HIV viral replication and pathogenesis and search for packaged host proteins in CHIKV capsids. This project proposes also to study the impact

of UNG2 depletion after HIV infection and/or VPR entry into B cells and again will take advantage of U 1058 cohorts;

- project 3 on traffic of CHIKV capsids in host cells and identification of capsid assembly sites in the infected cells. They will mainly use microscopy technics here to characterize CHIKV capsids induced spherules and the implication of the autophagy machinery in CHIKV replication.

The research plan dealing with viral capsid assembly and traffic in host cells is a hot topic that should lead to new antiretroviral compounds. All three topics are very ambitious, supported by state of the art techniques (electron microscopy, confocal immunofluorescence, 3D structure analysis...) but may be difficult to handle with the existing work force, and the strong but time consuming investment in teaching.

Conclusion

- **Strengths and opportunities:**

- the project is ambitious with high opportunities for valorisation;

- the experts committee warmly noticed the strong involvement in teaching, training and valorisation of their work.

- **Weaknesses and threats:**

- there are low to few collaborations or interactions with other teams working on the same field at the center level (MRR, MDVA) or at the national level (for capsid-host interaction either from HIV or CHIKV);

- the project will develop three different topics leading to increase risk of dispersion;

- there is a question on the feasibility of project 1, the biggest, which PI is deeply involved in teaching. However, the teaching activity must be maintained as it participates to the attractiveness and excellence of the team.

- **Recommendations:**

The experts committee strongly supports team VHI to follow its research plan but recommends increasing collaboration with other experts on capsid-host interaction to reach high impact factor publications. Especially the expertise of the team could be of great interest to study the role of capsid in the detection by the innate immune system of the incoming viruses. Finally, increase work force for project 1 might be considered to strengthen this ambitious project.

Team 6: Autophagy and infections (AI)

Name of team leader: Ms Martine BIARD-PIECHACZYK

Workforce

Team workforce	Number as at 30/06/2013	Number of 01/01/15
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	3
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**3**	**4**

Team workforce	Number at 30/06/2013	Number at 01/01/2015
Doctoral students		
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The team leader has an expertise on apoptosis and autophagy-mediated molecular mechanisms and was the first demonstrating that X4 env-expressing cells induce autopagic apoptosis in uninfected bystander CD4+ T cells. Thus, this group was the precursor of the following research on the role of autophagy on the replication and persistence of HIV produced also by other groups. Since 2008, during this evaluation period, they showed that this mechanism was not only limited to X4 envelope but also to that of R5 viruses, and more in specific showed that the gp41 fusion activity is the determinant of autophagy. This same mechanism was not induced in macrophages though. In macrophages, they demonstrated that autophagy was regulated differently by HIV R5 and X4. Since, they have continued to study the mechanism involded in HIV induced autophagy by analysing the interaction of viral proteins

and autophagic factors Atg, and showed that the viral protein vif binds to the Atg LC3 thus inhibiting autophagosome formation. The team has clearly shown a continuity in this reaserch field and has proceeded in deepening and unravelling the molecular mechanisms and pathways involved.

The team AI is a relative small group, which however has 2 permanent researchers and one permanent engineer. The team leader and the associated permanent researchers have an overall production since 2008 of 24 papers in peer review journals and 2 books chapters. The team has certainly an appreciable continuity in the production with 2 to 4 papers per year, with a standard of good quality. The most targeted journal is a high-ranked specialistic one (6 papers in Autophagy) and otherwise medium (PlosOne, Biochimie, Genet Evol, Curr Top Microbiol Immunol) or high rank journals (1 in Plos Pathogens) for a broader audience of readers. A considerable number of publications of the last few years are thanks to the previous and autonomous productivity of one new permanent staff member (CR1). A few publications are in collaboration with international research teams.

The experts committee agreed that the productivity of the team leader could improve, and that the productivity of the team in its whole has acquired an important contribution with the entry of one CR1.

Assessment of the unit's academic reputation and appeal

The team has good and appropriate collaborations with french and international (dutch, spanish and norvegian) research teams. The international visibility could improve.

The team members were invited or selected for oral presentations in national and international conferences on a regular basis.

The team has been involved in the co-organization of a few international Symposia in France. The team leader is a member of the Francophone Group of Autophagy (CFATG).

The team leader is teaching in M2 student courses at the Universités Montpellier and Marseille. Besides, during the evaluation period the team has attracted 3 PhD students: considering the small size of the team (one HDR) it is a valuable record.

The team has a regular financial support through french funding agencies (mainly Sidaction and ANRS).

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

The type of research does not imply interactions with social, economic and cultural environment. Indeed, there is also nothing specified in the dossier.

Assessment of the unit's organisation and life

The size of the team (1 DR2, 2 CR1, 1 IR2, and 2 PhD students) is appropriate for the research work performed, and planned for the future. The team is well composed with researchers of different levels of expertise and specificity.

Assessment of the unit's involvement in training through research

The team had 3 PhD students during the evaluation period, all are from France. The thesis was always completed in three years. All students have publications within their student-ship, although never as first name, and in some cases in papers headed by a scientist external to the team. The team has recruited 2 new PhD students for the coming period. Besides the mentoring of PhD students, they have a continuous flow of M2 students that they train.

The experts committee agreed that, considering the size of the team, they have a very good output of PhDs although the publication record and in specific the authorship could be improved.

Assessment of the five-year plan and strategy

Although the research plan for the future 5 years was not well structured and detailed in the written report, the presentation during the evaluation by the experts committee was well organized and clear. The team leader and the 2 staff members each presented their future work. The plan of the team for the future 5 years is consistent with their previous research line. They propose to deepen the knowledge in the mechanisms inducing autophagy in the

different cell populations involved in HIV infection as well as relevant players of innate and adaptive immune responses, such as DC, macrophages and neutrophils. They plan to explore the possibility to inhibit viral transfer to target cells through targeting the autophagosomal activity using rapamycin, and a collaboration with USA has been established for this part of the project. It is important to underline that the team has also planned to perform cohort studies to investigate the role of autophagy in disease progression of HIV/AIDS.

Conclusion

- **Strengths and opportunities:**

Future collaborations are in general well chosen. Two new PhD students were recruited in 2013, which shows the involvement and commitment of the team in training through research.

The experts committee agreed that the decision to recruit one promising young researcher with expertise in dendritic cell pathophysiology is seen as an important asset to the productivity of the group and will integrate well into the team's objectives.

- **Weaknesses and threats:**

Although the plan to investigate the role of autophagy in HIV patients cohorts is extremely relevant, it seems not well defined and the approach is still somewhat vague.

The team should also be aware of the increase in international competition in their field with new areas of research rising on the possible mechanisms exploited by HIV to induce bystander cell death.

- **Recommendations:**

The team has plans for the future to engage in new aspects and investigative approaches of autophagy, which should increase again their visibility. The team should consider also establishing collaborations with other internal teams, such as those dealing with tuberculosis, a disease in which autophagy plays a role. This would also make it possible to seek additional funding support.

Team 7: Players in the pathogenesis of the retroviral infections (PPRI)

Name of team leader: Mr Jean-Michel MESNARD

Workforce

Team workforce	Number as at 30/06/2013	Number of 01/01/15
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	4	4
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)	1	
TOTAL N1 to N6	**6**	**5**

Team workforce	Number at 30/06/2013	Number at 01/01/2015
Doctoral students	3	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs

The team PPRI firmly established its international position and reputation in the early 2000s (2002 onwards), with the seminal discovery of the HBZ gene of HTLV-1. HBZ is the only gene encoded on the negative strand of the provirus, and was the first new gene to be discovered in HTLV-1 for some 10 years. This paper qualifies as a citation classic, with over 250 citations. The discovery led to changes in our understanding of almost every aspect of HTLV-1: its persistence in the host, the pathogenesis of the associated diseases, and the role of the host immune response. In the decade since this discovery, the team has continued to exploit this niche, describing antisense-encoded transcripts in the related virus HTLV-2 and, more controversially, in HIV-1. In addition, the team has made several important contributions to elucidating the actions of the mRNA and the protein encoded by the HBZ gene. Finally,

the team has also made contributions to the study of HIV-1, including elucidating the mechanism of secretion of the Tat protein by HIV-1-infected cells.

In the period under review, the team has published 23 primary research papers, 4 reviews and 2 book chapters. It is noted that the team leader does not automatically add his name as a co-author to all publications arising from the group: this is appropriate and laudable. The majority of these publications are in highly respected, peer-reviewed journals of moderate impact, including Journal of Virology, Journal of Biological Chemistry, Retrovirology; a small number are in higher impact journals (Blood, Nucleic Acids Research), and members of the team are co-authors on 3 papers in first-rank journals (Cell, EMBO Journal).

The standard and quantity of published output are very good, and team members demonstrate the continued significant international profile of the team. The publications also demonstrate a good level of international collaborations.

In the recent 5-year period, their work has represented a logical extension and consolidation of the outstanding contribution they made in the previous 5-year period. The experts committee agreed that the team PPRI is still among the world leaders in the field of HTLV-1. The experts committee also considered that, given the originality of the work, the team could publish in higher-impact journals, which could bring their current work into the outstanding category.

Assessment of the unit's academic reputation and appeal

As is evident from the introductory remarks above, the team continues to enjoy a strong international reputation in the field of human retrovirology, as a result of the discovery and continued contribution to the understanding of antisense-encoded genes. The reputation of the team leader is also reflected by his roles on the Editorial Board of the journal Retrovirology and on the Executive Committee of the International Retrovirology Association, and his invitations to speak at international conferences in Canada, Italy, Austria,... The journal Retrovirology is continuing to rise in its international standing (impact factor), and is now the highest-ranking specialist journal in the field.

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

The work of the team is focused on basic research, and consequently this team does not make a strong or direct interaction with the social, cultural or economic environment.

Assessment of the unit's organisation and life

The scientific objectives of the team are clear, coherent and appropriate. The size of the team and its composition are also appropriate for the work currently undertaken and planned. The team is composed of 2 DR2 CNRS, 2 CR1 CNRS, 1 AI CNRS, 3 PhD students, 1 CDD IE, 1 postdoctoral fellow.

The team leader has appointed three subgroup leaders within the team and has well-defined and clearly expressed views on the trust that he places in each subgroup leader in the team. Each of the subgroup leaders presented a succinct summary of their planned work for the next 5-year period to the review committee. These presentations, and the introductory remarks by the team leader, conveyed to the experts committee a clear impression of a well-organized, happy and productive team.

Assessment of the unit's involvement in training through research

Considering the size of the PPRI team, it has a good output of research students. The team attracts good numbers of PhD students, the great majority of whom come from within France; in addition, the team contributes to teaching of Masters courses both locally, in Paris and in the Université des Antilles et de la Guyane. Nine PhD students were on the team during the review period, of whom 5 successfully defended a thesis and four are still in progress.

Assessment of the strategy and the five-year plan

The strategy of the team for the next 5 years represents a logical continuation of the work of the team on antisense proteins of retroviruses. Specifically, they plan to investigate the roles of antisense proteins in promoting viral persistence and in interfering with specific host cell functions such as differentiation, cytokine production,

intracellular trafficking, autophagy and antigen presentation. They also plan to investigate the use of antisense transcription as a marker of disease progression in both HTLV-1 and HIV-1 infections. In this work, they will continue to collaborate with clinical centers in Martinique, Guadeloupe and Cayenne (French Guiana). These collaborations are indeed essential to obtain the primary clinical material necessary for the experimental work, especially on the disease adult T cell leukaemia, which is rare in Europe.

The team will also follow their highly interesting and original recent findings on the secretion of HIV-1 Tat protein from infected cells, aiming to address both the mechanisms of secretion and the consequences for the infected cells and, perhaps more importantly, for bystander cells.

Conclusion

- **Strengths and opportunities:**

The proposed programme of research is logical and coherent, and makes appropriate use of the experience and expertise of the team members. The collaborations established with clinical units are a particular strength of the programme, and the team is encouraged to make maximal use of this valuable resource.

The experts committee recognized the originality of the team, and hopes that the team leader will continue to play a full part in the scientific direction of the team at the same time as taking up his role as deputy director of the new unit.

- **Weaknesses and threats:**

The team has clearly chosen to conduct projects with experimental objectives that follow directly from its recent work, which will make a useful contribution to the field, scientifically but may be relatively low-risk. The team is also encouraged to undertake new projects which are high-risk but potentially high-reward in particular in HTLV-1 biology.

- **Recommendations:**

The team has the opportunity, in the next 5-year period, to combine the scientific vision of the team members with the new resources offered by the collaboration with clinical colleagues in Martinique, to make further important contributions to the field, publish in high-impact journals, and achieve again in the outstanding range. The experts committee considers that, in view of the quality and originality of the research team, there is scope for inclusion in the 5-year programme of some higher risk projects in HTLV-1 biology, in addition to the somewhat higher-risk work currently underway in HIV-1 infection.

Team 8: Cellular biology of bacterial infections (CBBI)

Name of team leader: Mr Matteo BONAZZI

Workforce

Team workforce	Number as at 30/06/2013	Number of 01/01/15
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**3**	**2**

Team workforce	Number at 30/06/2013	Number at 01/01/2015
Doctoral students		
Theses defended		
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions		1

• Detailed assessments

Assessment of scientific quality and outputs

This is a recently created research team (January 2011) working in the field of host-pathogen interactions, mostly in Coxiella. A recent outbreak of Q fever in the Netherlands puts Coxiella on the stage and the discovery of virulence factors of this emerging pathogen is a hot research topic. Two recent facts have greatly facilitated this quest for virulence factors: the development of axenic culture media and improvements in the tools available for genetic manipulation. This is particularly well illustrated by the Tn library that the team started to construct and to validate in C. burnetii.

The two papers and the review published since the creation of the team are in well renowned journals in the cellular Microbiology field (1 Traffic, 1 Cell Microbiol, 1 Review in J Cell Biol, all as 1st author). These are still

publications resulting for the team leader post-doctoral period at the Pasteur Institute. In addition the overall ranking of the past publications from the team leader is excellent (Nat Cell Biol 2005, Cell Host Microbe 2010, J Cell Biol 2011, and several publications in Cell Microbiol).

Assessment of the unit's academic reputation and appeal

The team leader has a very good (international and local) visibility in the Coxiella field, as attested for instance by several invitations as a speaker at the American Society of Rickettsiology meeting. The team leader has been frequently invited to give seminars abroad, including in prestigious institutes (e.g. NIAID).

The team leader seems efficient in networking at the national and international levels. The ability to raise funds has been excellent (even with a private company, Sanofi) during the last three years; this includes an ATIP-Avenir fellowship.

The team recently recruited a high standard post-doctoral fellow from Imperial college (London) funded by a Marie Curie fellowship. An Infect-ERA-Net grant will allow hiring of a new post-doctoral fellow in the beginning of 2014.

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

A funding from Sanofi/Aventis R&D and Aviesan program is ongoing. A patent has been requested for a synthetic peptidic vaccine against Q fever.

Assessment of the unit's organisation and life

There are no data to give an opinion on this.

Assessment of the unit's involvement in training through research

The team leader is currently mentoring one PhD student and has trained 4 BTS, 1 Master and 1 Erasmus students. The PI will have its accreditation to direct research (HDR) in 2014.

Assessment of the five-year plan and strategy

Built on the expertise in constructing and validating a library of C. burnetii Tn mutants, the five-year project is original and ambitious and undoubtedly will lead to breakthroughs in the field of Coxiella pathogenesis. In addition to completing the coverage of the library, the following aspects of mutants characterization will be developped:

1/ adhesion and internalization with the identification and dissection of the pathway leading to invasion of non-phagocytic cells;

2/ cell to cell propagation of the bacteria;

3/ development of non-mammalian models (zebrafish and honeycomb moth);

4/ T4SS effectors and their eukaryotic partners co-opted by Coxiella to establish its replicative vacuole and to modulate apoptosis;

5/ non coding RNA identification;

6/ an original “conditional” system to synchronize the PV vacuole and screening of small molecules library to identify potential anti-infectious target or as surrogate of siRNA screen to identify host pathways.

The feasibility of the overall project is great if additional funding are obtained for the coming years.

Conclusion

- **Strengths and opportunities:**

The team leader is a clearly recognized expert in his field. The project is ambitious and original with a good balance of low risk and more risky/high reward tasks. The networking activity is excellent. The existence of a declassified Coxiella strain allowing to work in BSL2 conditions is a real strength and reduces greatly the bio-security administrative aspects. The developed tools and technics will undoubtedly create opportunities for additional fruitful collaborations.

- **Weaknesses and threats:**

In addition to the PI, the team is only composed of a post-doctoral fellow and of an assistant engineer (CNRS). The manpower capacity should be increased.

- **Recommendations:**

Fund raising should be intensified, and personal recruitment increased (including permanent and additional non-permanent staff).

Team 9: Bacterial Pathogeny and Anti-Infectious Strategies (BPAIS)

Name of team leader: Mr Stephan KÖHLER

Workforce

Team workforce	Number as at 30/06/2013	Number of 01/01/15
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	2
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**5**	**6**

Team workforce	Number at 30/06/2013	Number at 01/01/2015
Doctoral students	3	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs

The team BPAIS has a excellent background history in deciphering the adaptive potential of Brucella in response to various stresses. Moreover, due to its strong link with Germany (Federal Institute for Risk Assessment - BfR-, Berlin Germany), the team acquired an internationally recognized expertise in generating proteomic data in the context of Brucella both in culture and in infected cells (Proteomics 2008, BMC Genomics 2013). The team published the first proteomic analysis of intramacrophagic Brucella, giving to the community the first clues of the metabolic state of the bacteria and stresses conditions encountered in the Brucella containing vacuole (Proteomics 2008).This work is often cited.

Another research axis in which the team has gained international recognition is the anaerobic/microaerobic lifestyle of Brucella, usually considered as strictly aerobic. During this evaluation period the team produced a proteomic analysis of B. suis grown under these conditions and identified a two-component system (RegB/RegA) that plays an essential role (Proteomics 2009, Infect Immun. 2013, BMC Genomics 2013). There is almost no competitor on this field of Brucella research. The BPAIS team has been the first to characterize the pathogenic potential of a new species of Brucella (B. microti) isolated from the common vole and from the soil. This fast growing species was shown to be the only Brucella species able to kill its experimental host (mice) and to rely at least partially on the glutamic acid decarboxylase system for its oral infectivity in mice (J Infect Dis 2010, J Infect Dis 2011, J Infect Dis 2012). The field of characterizing the emerging Brucella species is quite competitive (even in France) actually. During the 2008-2013 period, the senior scientists of the team have published 15 peer-review publications including 7 articles in journals with impact factor higher than 4 in clinical microbiology, infectious diseases and proteomics (J Infect Dis, Infect Immun, BMC Genomics, Proteomics) and 1 book chapter as senior authors and 8 peer-review publications, 3 review articles and 1 book chapter as co-authors.

Concerning the interdisciplinarity, on the total of 19 peer- and non peer-review publications of the team during the evaluation period, 12 were made in relation with the identification of novel therapeutic targets against Brucella (or Mycobacterium) in a strong collaborative networking with PI from IBMM (Montpellier).

Assessment of the unit's academic reputation and appeal

In the last 5 years, the team has obtained a good national and international recognition in the field of Brucella molecular pathogenicity with 2 local and 1 national invited conferences, and with 6 invited international conferences. The team leader participated in organizing a national meeting in Montpellier in 2011. Two senior scientists of the team participated to 6 PhD-examination boards during the 2008-2013 period.

Almost half of the research grants (205 k€) for this team came from the BfR (Berlin Germany) and as such has implied a strong involvement of the team leader in this networking. At the national level, the team leader was also coordinator of an ANR grant 2009-2013 (343 k€ total, 226 k€ for his team). In summary, the good ability to raise funds from public entities in the past period underlines the potential of the group to self-sustain its research for the next 5 years.

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

The team leader co-holds one patent with an international extension (1 patent in 2008 with an international extension in 2010) about the use of inhibitors of histidinol dehydrogenase (Org Biomol Chem 2011). He has one advisor contract with the industry (Merck Darmstad) since 1992 on the development on Listeria diagnosis. One PI has participated to the Salon de l'Enseignement Supérieur in Montpellier every year since 2005. The team leader was also Directeur adjoint du CBPS between 2011 and 2013. Both these two PI participated in various local or national committees in the CBPS, in the Université Montpellier 2, in the AFSSET Agency, in the INSB department of the CNRS. One PI contributed to the writing of 3 scientific expert reports of the AFSSET.

Assessment of the unit's organisation and life

In 2008-2013, the group has included 3 senior scientists, 1 engineer, 3 post-doctoral fellows (with 1 having spent at least 12 months in the unit), 5 PhD students. Team meetings are organized weekly to discuss on-going projects.

Assessment of the unit's involvement in training through research

During the evaluation period, the team contributed to the formation of 3 post-doctoral fellows and 4 PhD students (with 2 co-directed by a member of the team) who graduated during the 2008-2013 period. Another PhD student, co-directed by a member of the team, will graduate later. The team leader participated to the MSc teaching in Universités Montpellier 1 and 2 in 2008-2011. The engineer of the team participated to CNRS training for BSL-3 confinement for industry.

Assessment of the five-year plan and strategy

As stated above, the continuation of the research on the characterization of the "microaerobic/ anaerobic" Brucella way of life is actually a niche that is almost free of competitors and in which the team has gained a clear expertise and a number of tools and technics. The evaluation of the persister state in this condition and the identification of the targets regulated by the TCS RegB/A will undoubtedly lead to data biologically relevant for the understanding of Brucella pathogenesis.

A second research axis, building on the gained expertise and collaboration with teams of structural chemistry, is the development of anti-infective drugs targeting the "stringent response regulator". The strength of this approach is both the previous knowledge of the Rsh system in Brucella, the availability of the in vitro and in vivo testing systems, the parallel that will be made with M. tuberculosis and the ongoing interdiciplinary collaborations. This is a clear example of effective association between basic and applied research.

The third point, consisting in RNAseq characterization of the newly described Brucella species by comparison with B. suis under acidic stress conditions and during macrophage growth is quite more risky. It is not clear how many new species will be investigated (and there are a lot of new ones). There is another French team working on the characterization of the pathogenic potential of these strains and probably some other international teams as well are looking at this aspect). In addition the amount of data generated by a RNAseq approach (on multiple strains, in multiple conditions compared to the classical B.suis strain) will have to be analyzed, this will imply a bioinformatic expertise that is not present in the team. Afterward, the relevant data will have to be biologically validated and this will required additional manpower.

Conclusion

- **Strengths and opportunities:**

The strategy plan for the next five years is in line with the recent achievements of this team and is consistent with the skills available both in the team and in the collaborative network. They will benefit from the technical facilities of the new research center (BSL-3 platform). The co-existence of teams working on other intracellular or chronic bacterial pathogens with thematic proximity is a clear opportunity for sharing equipments, knowledges and expertises. Their ongoing collaborations with structural chemists in Montpellier (IBMM) and the collaborator in Germany (BfR) will be a strong support to succeed in their projects. The link between basic and applied research is a clear opportunity of getting funded in a financial crisis period when funding agencies are putting the pressure on the socio-economic impact of the research.

- **Weaknesses and threats:**

The necessity to work under BSL3 conditions and the "administrative load" involve an incredible amount of time-consuming work. Even if the search for new therapeutic targets is a funding opportunity, this is an applied research giving "alimentary resources". There is a need of basic Brucella researches and the expertise of the team has to be preserved. The manpower is quite limited so as the number of PhD students and post-doctoral fellows.

There is no collaboration with the French National Reference Center for Brucella (Anses, Maison-Alfort) and its associated lab in Université Montpellier (INSERM U 1047 located in Nîmes), except the co-direction of 1 PhD student between one PI of the team and the director of U 1047.

- **Recommendations:**

In conclusion, more post-doctoral fellows and more PhD students should be recruited. Bioinformatic expertise in the team will be necessary for one of the 3 projects of the team.

Team 10: Diagnostic and Therapeutic Innovation (DTI)

Name of team leader: Ms Chantal FOURNIER WIRTH and Mr Edouard TUAILLON

Workforce

Team workforce	Number as at 30/06/2013	Number of 01/01/15
N1: Permanent professors and similar positions	8	7
N2: Permanent EPST or EPIC researchers and similar positions	3	3
N3: Other permanent staff (without research duties)	8	9
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	4	3
N6: Other contractual staff (without research duties)	5	4
TOTAL N1 to N6	**28**	**26**

Team workforce	Number at 30/06/2013	Number at 01/01/2015
Doctoral students	4	
Theses defended	6	
Postdoctoral students having spent at least 12 months in the unit	4	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	6	8

• Detailed assessments

Assessment of scientific quality and outputs

Team DTI unit is a merging between the previous TransDiag (a local research laboratory from the National Blood Banking) and a part of the former INSERM U 1058. In the past 5 years, the new team co-directors have published or been associated with 8 and 27 publications respectively, including first rank journals (Blood, J Immunology, Hepatology).

U1058 publication activity is impressive with 197 original articles in the last 5 years including some in major reviews (Lancet, British Medical Journal, Blood, Journal of Immunology, Hepatology, Clinical Infectious Diseases). Team DTI will inherit a major blood specimen collection derived from a large network in developing countries.

TransDiag created 12 years ago has developed new technologies as ELOSA and patented polythiolated probes for a large molecular screening of viruses in blood transfusion medicine.

Assessment of the unit's academic reputation and appeal

TransDiag remains attractive for senior scientists, recently recruiting two major national researchers in the field. U 1058's major epidemiological expertise in HIV cohort monitoring and international university partnership is demonstrated by publications in high ranking review journals.

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

The researchers from U 1058 created the start-up OMUNIS on January 2014. This company is attempting to develop and commercialize innovative diagnostic tools for infectious chronic diseases (hepatitis C, TB). TransDiag has in recent years registered four patents in innovative diagnostics and was also active in the field of non-conventional agents with 5 on-going academic or industrial contracts including collaborative studies with United Kingdom. U 1058 researchers created a start-up to promote and commercialize their innovative diagnostic tools for chronic diseases with support from the Region. U 1058 recruited a communication officer to organize the communication with the regional, national and international media and has developed a broad strategy to publicize the work in different media.

Assessment of the unit's organisation and life

The new DTI "Diagnostic and therapeutic innovation" is a joint management co-directed by PI from TransDiag and the U 1058 unit. It is composed of 7 senior scientists and four medical biologists (PH) who provide the drive for translational research. The team proposes to develop new concepts and new tools for diagnosis and therapeutic innovation. TransDiag and U 1058 will combine excellent technical knowledge, clinical medical expertise in diagnosis and management, and a rich panel of samples. This is one of the most important teams of the new organization in terms of human resources but the new team will remain separate in terms of the location of their laboratories. The researchers who come from the U 1058 will remain located in their university hospital laboratories.

Assessment of the unit's involvement in training through research

As a new branch, any evaluation is somewhat premature, but the combined potential of the partners has been previously proved as highly valuable for teaching: special mention must be made of the training of young scientists from Developing Countries (DC). The new organization will open wider opportunities for translational researchers particularly for the post-doctoral development in new generation technologies. Seven PhD theses have been defended and 9 are ongoing in U 1058.

Assessment of the five-year plan and strategy

Three major activities are planned: innovative diagnostic concepts, therapeutic innovations and biological collections. The strategy is clear, with a progression from proof-of-concept to partnership with industry according to the success of the new assays proposed by team DTI. The team will have access to a large range of pathogens, from parasites to prions, to develop the new assays. The objective will be to select a limited number of targets and to evaluate and validate one or two new assays at five years.

1/ One of the main strategies is to develop diagnostic tests for the simultaneous detection of different infectious agents. Introduction of new sophisticated technology such as the polythiolated probes, patented by TransDiag, could be a key feature in this new multiplex approach and the panel of stored samples like Dried Blood Spots will allow evaluation of such tools. The team has the expertise to overcome the numerous difficulties in such technical development. The project to develop serological monitoring to identify active tuberculosis is a risky gamble, but the team has the skills and resources to evaluate these new tests.

2/ Data on therapeutic innovations are too limited to be evaluated at this stage. For example, the proposed study of the ability of anti-retroviral drugs to control endogenous Reverse Transcriptase activity in psoriasis is largely hypothetical. It was still unclear following the meeting evaluation if this activity will remain in team DTI or will be devoted to team TCCI.

3/ The biological sample collection of this team is impressive and a strength for the future.

Conclusion

- **Strengths and opportunities:**

The contribution of TransDiag and patents on new probes should allow multi-genomic detection of blood-borne viruses. To implement and to manage a large and documented sample collection is a strength. This biobank could lead to the evaluation of new potential surrogate markers for diagnosis and therapeutic monitoring in various diseases. The same is true for the powerful network developed by the U 1058 in developing countries allowing the team to perform large field evaluations.

- **Weaknesses and threats:**

Objectives need to be better defined with a limited number of topics and a short list of pathogens to be studied. Team DTI should select only a short number of questions to be credible. Research on such a large panel of pathogens represents excessive dispersion. This is a limiting factor for this team DTI who should focus on a more limited number of infectious diseases.

- **Recommendations:**

The experts committee suggests that the future team DTI applies its expertise to a limited number of pathogens with simple and achievable objectives, such as the development of certain tests for easier molecular monitoring. There is a major potential for excellence in this team if they define clearly their project to develop innovative diagnostic concepts. It is highly challenging to compete with big manufacturers with new innovative assays for the major public health threats like HIV, Flu or TB. The team is particularly encouraged to develop simple hepatitis C monitoring in developing countries. HCV therapy in southern countries will encounter the same limitations as those for HIV for whom U 1058 is well-experienced. Neglected diseases also badly need new diagnostic tools and the vast experience in the clinical study management of the team and Axis 3 scientists in developing countries are invaluable for this kind of challenge.

Team 11: Transmission and Control of Chronic Infections (TCCI)

Name of team leader: Mr Nicolas NAGOT

Workforce

Team workforce	Number as at 30/06/2013	Number of 01/01/15
N1: Permanent professors and similar positions	6	7
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	3	4
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		1
N6: Other contractual staff (without research duties)	4	2
TOTAL N1 to N6	**15**	**16**

Team workforce	Number at 30/06/2013	Number at 01/01/2015
Doctoral students	3	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	7	8

• Detailed assessments

Assessment of scientific quality and outputs

Team TCCI, "Transmission and Control of Chronic Infections" is the result of a merging of one part of the INSERM unit U 1058 - "Infection by HIV and by agents with muco-cutaneous tropism: from pathogenesis to prevention » IHAMT, and previous team 7 from the CPBS. This team 7 of the CPBS worked on the identification of molecular determinants of innate antiviral immunity, demonstrating significant scientific excellence given its small size (made up of only 2 researchers and an ITA). Its research focused on cellular factors involved in the control of replication of some RNA viruses including retroviruses HIV-1 and HTLV-1. The main results are the identification and characterization of the ubiquitin ligase TRIM22 as a major actor of the IFN-mediated antiviral response against RNA

viruses (publications in Futur Virol., J Virol/ Virology/ J Gen Virol). In August 2013, the unit U 1058 was composed of 40 people, among them only one full-time researcher and 14 hospital-university employees. The activity of this team is organized around 3-principle research axes as follows: transmission and prevention of HIV, interactions between HIV and other infectious agents, and viruses with muco-cutaneous tropism. Axis 1 has 2 main goals that include understanding the mechanisms of HIV-1 transmission through breastfeeding, and identifying innovative prevention tools. The ultimate goal is to adapt their findings to a large-scale implementation and to the characterization of HIV reservoir in the genital compartment in order to prepare the evaluation of new prevention tools against sexual transmission of HIV-1. This research team initiated numerous studies as investigators and coordinators. Some of them consisted of large-scale prevention trials conducted on infants in several African countries, as for example the PROMISE consortium, and clinical studies with high-risk women in Burkina-Faso. These studies provided some very significant results in the field of HIV transmission, which influenced the international and national guidelines and the management of primary and secondary HIV transmission in high-risk populations. The U1058 scientific production has been impressive and highly significant, reaching 386 original articles in high-ranked journals in 5 years (from 2008 to 2013), of which 230 are related to topics of Team TCCI (publications in AIDS, Pediatr Inf Dis J, AM J Epidemiol, Emerg Infect Dis., PLOs One, …).

Assessment of the unit's academic reputation and appeal

The team U1058 enjoys national and international recognition as investigator and coordinator of major clinical trials in the field of HIV infection. The INSERM unit 1058 is a founding member of the Labex EpiGenMed. The former team leader has been designated expert for the NIH, and has been invited by the EDCTP (EU) for two expert meetings on HIV and tuberculosis in 2013. U 1058 is largely supported by ANRS and others funding and in particular is coordinating a major EU-ANRS project PROMISE PreP (ANRS 12174) (to compare two different regimens of anti HIV prophylaxis for the children).

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

The unit U1058 comprises a communicator officer, who serves as a link between the community and associations of HIV infected people inside the international network, and supervises the communication with the regional, national, and international media. The ANRS organized in 2013 a press conference to broadcast the important results of the clinical trial infant PreP to prevent breast milk HIV-1 transmission. The magazine “La Recherche” elected the clinical trial Promise-PEP as one of the ten most important scientific discoveries in 2013.

Assessment of the unit's organisation and life

The newly formed team TCCI will be led by Mr Nicolas NAGOT (MD, PhD, MCU-PH), who works at the Nouvelle Université de Montpellier (NUM) as epidemiologist. This team will include seven senior researchers (2 full time researchers –ie 1 DR CNRS and 1 CR1 INSERM-, and 5 research professors from the NUM). The former team leader will instead become the director of the new Research Center on Chronic Infections. The team 7 of the CPBS, which has a basic research approach, will be integrated into this new team primarily involved in translational and clinical research.

The gathering of all research teams into one geographical location provides a major advantage for the dynamics of the projects. The working principle set forth is to favour the multiple exchanges between researchers through flexible governance, to create a synergy allowing for excellence in scientific production, and to assure strong understanding between the individuals sharing the same space. This principle has proven its potential from within the unit U1058. Its leader is confident in its future application within the developing project.

Assessment of the unit's involvement in training through research

U 1058 team members have trained 7 PhD students since 2008 and are highly involved in teaching activities by giving lectures to medical students at the Université Montpellier. The team has developed significant teaching activity and training courses in resource-limited countries. The different research programs are impressive. Two PhD are currently being supervised by members of Team TCCI. The attractive qualities of this team will undoubtedly increase the attractiveness and integration of new doctoral candidates.

Assessment of the five-year plan and strategy

The global project of this team over the next five years will focus on HIV while offering also studies on other chronic infections (Hepatitis C, HPV, and cancer). Some of these are innovative and also more risky (evaluation of anti-retrovirus in the psoriasis, research of polyomaviruses in the genital tracks).

The projects focusing on infection by HIV-1 operate at three levels. The first level concerns public health and is organized around the axes of primary and secondary prevention of transmission of HIV-1. This part is a continuation of ongoing projects (PROMISE-PEP, DRIVE, cohorte FSW Burkina Faso), which are supported by various sources of funding and are doubtless outstanding and excellent projects. The elaboration of future projects is currently in process. This work is to be complemented by studies of the transmission of HIV-1 at the individual level (determining the factors involved in the innate immune response) with samples collected during clinical studies. This work is not yet clearly planned and outlined in a precise manner. No clear project has been presented for the former team 7 of CPBS, as currently, and no specific mutual collaborative project is scheduled.

Conclusion

- **Strengths and opportunities:**

This team has extensive experience and masters its subject of study. Its working fundaments are excellent and there is no concern about the possible sources of funding. The future team leader is a young epidemiologist, who is well integrated into existing projects and has a good understanding of collaborative networks established with Africa and Asia. The collaboration with other research teams within an organization is, in principle, a stimulating synergistic factor.

- **Weaknesses and threats:**

There are only a few minor remarks about the project of this team. These mainly concern the integration of the former team 7 of CPBS, as currently, no specific mutual collaborative project has been proposed. Similarly, collaboration of Team TCCI with the other teams in the research center is not yet clearly visible.

- **Recommendations:**

The first recommendation is to ensure the continuity of the excellence of this team and its many strengths. The proposed future project plans raise the need for strengthening the immunological research of this team. The recruitment or collaboration allowing a better continuum between fundamental research and clinical research, and a synergistic scientific production, is recommended. Furthermore, a clear position of the former team 7 of CPBS should be proposed.

5 • Conduct of the visit

Visit dates:

Start: January 27th 2014 at 09.00 am

End: January 29th 2014 at 05.00 pm

Visit site: CNRS

Institution:

Address: Route de Mende, 34000 Montpellier

Specific points to be mentioned:

Agenda of the site visit

Center for Chronic Infections
Proposed director: Mr Philippe VAN DE PERRE

AERES scientific delegate (DS): Ms Sophie DE BENTZMANN

Experts committee: Ms Elisabeth MENU, Mr Olivier NEYROLLES, Mr Jean-Jacques LETESSON, Ms Cécile BEBEAR, Mr Charles BANGHAM, Mr Gilles MIRAMBEAU, Mr Philippe BENAROCH, Ms Astrid VABRET, Mr François SIMON, Ms Hélène DUTARTRE, Ms Gabriella SCARLATTI

Day one – 27th January 2014

Room rental: Amphithéâtre de la Délégation Régionale CNRS (route de Mende)

09.00 am	Welcome (closed door) experts committee with the DS
09.15 am	DS: the role and procedures of AERES
09.30 am	Direction of the center: past and future
10.30 am	coffe break
10.45 am	Team Bacterial Enzymes and Resistance to Antibiotics Team leaders: Ms Corinne LIONNE & Mr Konstantin BRODOLIN
11.40 am	Team Mycobacterial Pathogenesis and Novel Therapeutic Targets Team leader: Mr Laurent KREMER
12.35-12.45 pm	closed meeting
12.45 pm	lunch
01.30 pm	Team Bacterial Pathogeny and Anti-Infectious Strategies Team leader: Mr Stephan KÖHLER
02.25 pm	Team Cellular biology of bacterial infections Team leader: Mr Matteo BONAZZI
03.20-03.30 pm	closed meeting
03.30 pm	coffee break

03.45 pm	Parallel meetings with personnel: - discussions with engineers, technicians and administrative; - discussions with staff scientists; - discussions with students and post-docs.

Day two: 28th January 2014

Room rental: Amphithéâtre de la Délégation Régionale CNRS (route de Mende)

08.30 am	Team Metabolism of retroviral RNA Team leader: Ms Marylène MOUGEL
09.25 am	Team Membrane Domains and Virus Assembly Team leaders: Ms Delphine MURIAUX & Mr Cyril FAVARD
10.20-10.30 am	closed meeting
10.30 am	coffee break
10.45 am	Team Virus-Host Interactions Team leader: Ms Laurence BRIANT
11.40 am	Team Autophagy and infections Team leader: Ms Martine BIARD-PIECHACZYK
12.35-12.45 am	closed meeting
12.45 am	lunch
01.45 am	Team Players in the pathogenesis of the retroviral infections Team leader: Mr Jean-Michel MESNARD
02.40 am	Team Diagnostic and therapeutic innovation Team leaders: Ms Chantal FOURNIER WIRTH & Mr Edouard TUAILLON

Presentation of the CEMIPAI platform hosted in CPBS (Mr Christian DEVAUX)
Presentation of OMUNIS, a start up enterprise hosted in the INSERM unit 1058 (Mr Pierre-Alain RUBBO and Mr Jean-François BLOCH)

04.05-04.15 am	closed meeting
04.15 am	coffee break
04.30 am	Team Transmission and control of chronic infections Team leader: Mr Nicolas NAGOT
05.25-05.30 am	closed meeting

Day three: 29th January 2014

Room rental: Salle des Colloques de la Délégation Régionale CNRS (route de Mende)

09.00-09.30 am	Discussion with the representatives of the managing bodies
09.30-10.00 am	Enlarged discussion with the partners
10.00-10.15 am	Discussion with Doctoral School director
10.15-10.45 am	Discussion with the head of the center
10.45 am	Coffee break
11.00-05.00 pm	Private meeting of the experts committee (in presence of the DS) including Lunch
05.00 pm	End of the visit

6 • Supervising bodies' general comments

Université Montpellier 1

AES Droit, Sc. politique Économie IPAG ISEM Médecine Odontologie Pharmacie STAPS

nouvelle université de Montpellier
un projet, une ambition

Monsieur Didier HOUSSIN
Président de l'AERES
Monsieur Pierre GLAUDES
Directeur de la section des unités de recherche
Agence d'Evaluation de la Recherche et de l'Enseignement Supérieur (AERES)
20, rue Vivienne
75002 PARIS

Montpellier, le 31 mars 2014

Référence : Ph. VAN DE PERRE/ Ch. DEVAUX : S2PUR150008534 CRIC Centre de Recherche sur les Infections Chroniques. 0342321N

Messieurs,

Je tiens à remercier le comité de visite AERES pour la qualité de son rapport d'évaluation concernant l'UMR 5236 dirigée par M. Christian Devaux et l'U1058 dirigée par M. Ph Van de Perre qui ont pour objectif de fusionner pour créer le Centre de Recherche des Infections Chroniques (CRIC).

J'ai bien noté les remarques formulées par le comité de visite et je veillerai à ce que celles-ci soient prises en compte par le directeur de la nouvelle structure de recherche.

Vous trouverez ci-joint les corrections factuelles et les observations générales formulées par le directeur.

En tant que tutelle Universitaire, je souhaite apporter mon soutien à ce projet de création du CRIC qui présente un intérêt structurant majeur pour la recherche en infectiologie de notre site.

Je vous prie d'agréer, Messieurs, l'expression de mes salutations les plus respectueuses.

Philippe Augé
Président
Université Montpellier 1

Comments

First, we would like to acknowledge the fantastic work of the AERES Expert Committee. The comprehensive, broad evaluation and the accuracy of the recommendations will be the cornerstones of our future Research Centre. We would like to collectively warmly thank all Expert Committee members, in particular its Chair, as well as the Scientific Delegate representing AERES and all representatives of managing bodies and partners for the quality of their expertise and their commitment.

We only have a very limited list of comments.

- Page 13, “The director and vice-director were elected by a consensus”: In fact, the future director and vice-director have been formally elected by both laboratory councils (of UMR 5236 and Unit 1058).

- Page 14: We are extremely satisfied by the commitment and appreciations of the potential management bodies and have great hopes in the involvement of CRNS (principal management body), NUM, INSERM and EFS as “co-tutelles” with a strong collaboration agreement with CHRU Montpellier.

- Page 15, chapter “Weakness and threats”: “The experts committee has noticed that there is not enough collaboration between the teams within the center”.
  In fact, since the beginning of the preparation of the project (about a year ago), after an understandable period of “knowing each other’s personality and professional skills” several collaborative projects between CPBS and Unit 1058 have been launched, for example on autophagy and the HAMLET complex (between AI and DTI/TCCI), autophagy in HIV Elite controllers (between AI and DTI/TCCI), on anti-infectious peptides (between VHI and DTI/TCCI), the presence of anti-ASP in breast milk of HIV-infected women (between PPRI and TCCI), the anti-infectious properties of Langerhans cells (between AI and TCCI), the encapsidation of HIV DNA in HIV-infected individuals (between MRR and DTI/TCCI) and the infection of keratinocytes by Chikungunya virus (between VHI and TCCI, manuscript submitted). Three collaborative projects have already been submitted for funding, two to ANRS and one to PHC-13 of Horizon 2020. We consider this as extremely encouraging signs of future collaborations between teams within the center.

- Page 15 and 16, chapter “Recommendations”: We endorse all suggestions and are grateful to the AERES Expert Committee for the very relevant and useful recommendations. Some of them have already been pursued. For example, we are actively seeking for additional expertise in immunology, with some possible new comers in the field of immunosenescence related to chronic infections. Also, introducing the new system of mentorship has been welcomed as a great idea that could be launched via the opinion leaders of the 3 scientific axes. A clear position for the CEMIPAI platform will be discussed with CNRS in the very near future.

- **Team 2 (MDVA)**: The scientific production of this team is improving rapidly, as exemplified by two recent publications published after the AERES Expert Committee visit:

  - L. Charlier, M. Louet, L. Chaloin, P. Fuchs, J. Martinez, D. Muriaux, C. Favard* & N. Floquet*. Coarse Grained Simulations of the HIV-1 Matrix Protein Anchoring: revisiting its assembly on membrane domains. *Biophys. J.* (2014) *106(3),pp 577-585*.*co-last.
  - C. Faivre-Moskalenko, A. Thomas, K. Tartour, J. Bernaud, Y. Beck, M. Iazykov, J. Danial, M. Lourdin, D. Muriaux* & M. Castelnovo*. RNA control of HIV-1 particle size polydispersity*. PLOS one* (2014) *in press*.*co-last. .

  The two PhD candidates who had applied for a PhD grant were successful and joined the lab in October and December 2013, respectively. The same is true for two post-doc candidates who will join MDVA during the year 2014.

  In addition, collaborations have been set up with other teams both internal to CPBS (with Team 3 (BERA) , see Kerviel A et al, Virus Research 2013) and external with IBMM (see Charlier L et al. Biophys J 2014).

- **Team 10 (DTI**): Team 10 members fully endorse the evaluation and are grateful to the AERES Expert Committee for its very encouraging evaluation and recommendations. In particular the team is ready to concentrate on a work plan on achievable objectives focused on a limited list of relevant pathogens, HCV being at the frontline. The only remark is on the fact that team 10 has not been working so far on flu and has no intension to do so in the future.

- **Teams 10 and 11 (DTI and TCCI)**: The projects on the possible involvement of endogenous retroviruses in the pathogenesis of psoriasis and on repurposing of antiretroviral drugs for psoriasis therapy are clearly collaborative between DTI and TCCI. Since the AERES committee visit, two proposals have been submitted one to ANRS and the other to Horizon 2020 PHC-13-2014.