



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

Research Units Department

AERES report on unit:

Virus-host interactions and liver disease

Under the supervision of the following
institutions and research bodies:

University of Strasbourg

INSERM



January 2012



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

Section des Unités de recherche

Le Président de l'AERES

Didier Houssin

Section des Unités
de recherche

Le Directeur

Pierre Glaudes

Unit

Name of unit:	Virus-host interactions and liver disease
Acronym of unit:	
Label requested:	UMR_S
Present no.:	UMR_S748
Name of Director (2009-2012):	Mr Thomas BAUMERT
Name of project leader (2013-2017):	Mr Thomas BAUMERT

Members of the committee of experts

Chair:	Mr Fabien ZOULIM, Lyon (representative of CNU)
Experts:	Mr Volker LOHMANN, Heidelberg, Germany
	Mr Salim KHAKOO, London, United Kingdom
	Mr Matias AVILA, Pamplona, Spain
	Mr Michael KANN, Bordeaux
	Mr Didier SAMUEL, Villejuif (representative of INSERM)

Representatives present during the visit

Scientific Delegate representing AERES:

Mr Jean ROSENBAUM

Representative(s) of the unit's supervising institutions and bodies:

Mr Eric WESTHOF, University of Strasbourg

Mrs Marie-Josèphe LEROY-ZAMIA, Inserm



Report

1 • Introduction

Date and conduct of visit:

The visit took place on January 12, 2012 in the Forum of University of Strasbourg. The lab director gave first a general overview of the laboratory and a presentation of the scientific program. This was followed by short presentations of other staff scientists. The committee then met University and Inserm representatives, and split for separate meetings with PhD students/post-docs, technicians, and scientists.

It should be noted that Mr Matias Avila could not take part to the site visit.

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

This is a mixed INSERM-University research unit which is located in Strasbourg. It was created five years ago with the recruitment of Prof Baumert from Freiburg, Germany, with a position of PU-PH and head of the laboratory. This was part of the restructuration of a previous Virology INSERM Unit.

The research program of the unit is focussed on hepatitis C virus - host cell interactions, pathogenesis of hepatitis C infections, mechanism of viral entry, and discovery of viral entry inhibitors with the aim of providing innovative medicine for the treatment of hepatitis C in clinical practice.

Unit workforce:

Workforce	Number on 06/30/2011	Number on 01/01/2013	2013-2017 Number of producers* *
N1: Professors or assistant professors	4 (2 FTE)	4 (2 FTE)	4
N2: EPST or EPIC researchers	3 (2.5 FTE)	3 (2.5 FTE)	3
N3: Other professors and researchers	2	0	0
N4: Engineers, technicians and administrative staff *on a permanent position	15 (13,9 FTE)	16 (15,8 FTE)	
N5: Engineers, technicians and administrative staff * on a non-permanent position	5		
N6: Postdoctoral students having spent at least 12 months in the unit	7		
N7: Doctoral students	13		
N8: PhD defended	4		
N9: Number of Habilitations to Direct Research (HDR) defended	3		
N10: People habilitated to direct research or similar	8	7	
TOTAL N1 to N7	49 (46,4 FTE)	23 (20,3 F)	7

* If different, indicate corresponding FTEs in brackets.

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

Definition and downloading of criteria:

<http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-unites-de-recherche/Principes-d-evaluation>.



2 • Assessment of the unit

Overall opinion on the unit:

The committee agreed that the unit has an outstanding activity in the field of HCV - host interactions at the level of both basic science and translational research. The director and his collaborators have created a unit which is internationally recognized in the field. The quality of the science, publications, fund raising and governance are excellent.

Strengths and opportunities:

The unit has developed all of the required technologies, study models and platforms to perform its research projects in a highly competitive manner. The unit's program is based on complementary approaches from basic science to clinical application and valorization.

Doubtless the unit is one of the world leading laboratory in the field of HCV entry inhibition. Their projects will be highly competitive and will provide important and new information on several aspects: 1) basic science knowledge of the mechanism of viral entry, 2) drug discovery and clinical trials of HCV entry inhibitors, 3) understanding of HCV pathogenesis based on translational research programs with application for liver transplant patients (prevention of graft infection). Moreover, their work on neutralizing monoclonal antibodies seems to be successful not only in acute infection but also in chronic infection models and is therefore promising in terms of clinical applications.

The unit has shown a large number of high quality results and has been extremely productive during the last evaluation period (publications in high ranking journals). As a result, the unit was able to recruit young talented researchers on INSERM or University positions.

The unit was also very competitive and successful in fund raising in the most competitive national calls (« investissement d'avenir ») and EU calls (ERC, InterReg).

Weaknesses and risks:

The unit proposal comprises a number of risky projects including a drug discovery and development project on HCV entry inhibitors, a program on host factor discovery in HCV entry, and the development of a mouse model, which all could lead to breakthroughs in the field. The quality of science and preliminary results render these projects realistically feasible. In any case, these projects will generate very important information on the biology of HCV and its interaction with its host. The unit is perfectly aware of these risks and has developed less risky projects for which preliminary results suggest a high level of feasibility.

No significant weakness was identified by the committee.

Recommendations:

The recommendation of the committee was to continue the same strategy.



3 • Detailed assessments

The unit presents a nicely integrated research program that is focused on the study of the pathogenesis of hepatitis C infections, the mechanism of viral entry, the discovery of viral entry inhibitors and is based on complementary approaches. The program has many clinical applications which follow well integrated translational studies.

Assessment of scientific quality and production:

The research program of the unit is focused on the study of HCV-host interactions, which is a very competitive research area. The unit is recognized as one of the world leading laboratories in HCV entry and pathogenesis due to highly relevant research and important contributions to the field of HCV infections. Recent seminal contributions of the unit include: (1) the discovery of viral entry and evasion from antibody responses as key factors for pathogenesis of liver graft infection; (2) the identification of specific cellular protein kinases as novel host factors regulating HCV entry; (3) the development of HCV entry inhibitors based on small molecule kinase inhibitors, as well as on neutralizing monoclonal antibodies targeting cellular HCV receptors. Characterization of the interaction of a viral nonstructural protein with apolipoprotein E and clarification of the role of neutralizing antibodies in viral clearance are further examples of important results with high international impact. Overall, the unit provides original and competitive research on the study of the mechanism of HCV entry and propagation and on the development of new entry inhibitors at the highest international level. The results are of highest impact on basic science with strong translational aspects, including the development of novel therapeutics based on own research, which will enter an investigator-initiated phase I clinical trial supported by INSERM and Roche.

The productivity of the research unit is outstanding, both in quantity and quality. Since 2007 the unit has published a total 109 original research papers in peer reviewed journals (42 directly from the unit with first and/or last author from the team), 31 (12 directly from the unit) with an IF > 5 and 20 (11 directly from the unit) with an IF > 10. The high international visibility is exemplified by recent publications in *Nature Medicine* (2011) and in the *Journal of Experimental Medicine* (2010), which were associated by comments and editorials in various journals and the media, and by two publications in *PNAS* (2007 and 2008). The publication record furthermore includes a number of papers directly originating from the unit in top journals of the respective field like *Gastroenterology*, *Hepatology*, *Journal of Hepatology* and *Journal of Virology*. The unit is also keen to present its results to a broader community by contributing to a total of 45 review articles in peer reviewed journals including an article in *Nature Reviews Microbiology* (2010).

In summary, the scientific quality and production of this unit is outstanding, documented by a very large number of high impact publications.

Assessment of the unit's integration into its environment:

The unit is extremely well integrated into the local and regional research structures. Currently seven patent applications have been submitted, 50 contracts for materials have been signed, 12 company contracts and an OSEO award to create a start-up company have been received. The unit is excellently integrated in hospital structures such as the departments of Virology and Hepatology, but also in the University, enabling the set-up of an MD/PhD position as part of their Laboratoire d'Excellence award (Hepsys). As part of their research, a well-working collaboration with the "Institut de la Souris", Strasbourg, was established. One team member has an appointment within the Laboratory of Virology within the Hospital. Collectively, these links are extremely helpful in facilitating the translational research program of the unit.

On the regional level the unit is a coordinating partner in the EU-funded Hepato-Regio-Net program linking the University of Strasbourg with Freiburg University and Basel University, and also part of the ERC Hepcent collaboration with the University of Heidelberg and Inserm UMR_S 758. The unit has additional funding as part of the Europrise network for HIV. ANRS funded collaborations include programs of "mouse models for viral hepatitis" and "HIV neutralising antibodies". This collaborative outlook has led to the unit being highly successful in attracting external funding which amounts to more than Eu10m (>Eu4m from European programs, >Eu4.5m from Science of Excellence « Investissements d'Avenir » programs and >Eu3m from National programs) from the last five years.

Their work is supported strongly by the University of Strasbourg with many staff positions including technicians and MCU-PH positions. Recently a CR1 position was obtained from INSERM (see also below).



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

The unit has an excellent national and international reputation. The director was awarded a "Chaire d'excellence" from ANR. The unit was successful in the highly competitive calls of the "Investissements d'Avenir" program since they were awarded a Laboratoire d'Excellence (LabEx) "Hepsys" and they are partner on another LabEX on HIV "VRI". Senior researchers have been invited many times to give lectures in international conferences or international institutions.

The laboratory is very attractive as exemplified by the training of in average 13 PhD students each year, 10 post-docs; but the unit has also trained 3 visiting senior scientists. Because of the high quality of research and funding from EU (InterReg program and ERC), approximately 2/3 of the trainees came from abroad.

As a result of the excellent quality of the research and scientific production as well as the performance of the trainees, the unit was able to obtain two recent researcher positions: one CR1 was recruited in 2009 at INSERM and one MCU-PH in 2011 at the University.

Based on an outstanding scientific reputation, the unit was able to join strong national networks supported by ANRS (HIV neutralization ; Hepatitis mouse model) and to establish international networks especially via EU funded programs (ERC, InterReg) or INSERM (European Associated Laboratory with Freiburg University). Furthermore, they have established 8 active international collaborations (examples : Rockefeller University, Tokyo, Scripps Institute, Birmingham University, Harvard University) with supporting publications.

Assessment of the unit's governance and life:

The unit's research program is based on a very well structured program with four thematic groups on virus-host interactions, lipoproteins and HCV life cycle, viral evasion and liver disease, HCV-HIV co-infections, and two platforms for animal models and for translational research.

There is strong leadership from the director, and one senior scientist has been promoted to deputy director of the unit. The management structure is well organized comprising a Unit Board (Conseil de laboratoire) which includes representatives from all levels within the unit. The unit further has a good internal and external communication strategy.

Scientific activity is well stimulated as shown by the quality of the outputs. Specifically the unit meetings are supplemented by a bi-weekly journal club, monthly invited speakers and scientific symposia, which are integral to the European grant structures. Additional educational activities include undergraduate laboratory training, seminars for the general public and media releases.

The depth of funding allows the group to be able to take a number of risks. This is best illustrated by the the mouse models of HCV infection, which is a challenging project. To address the risk the group has set up scientific collaboration with a well-known expert group, and having several contingencies, they are including alternate models to increase the probability of project success.

To supplement the unit's educational needs there are weekly unit meetings, weekly thematic group meetings, monthly working group and staff scientist meetings and bi-annual unit board meetings. They are involved in structuring regional research through the trans-border FP7 funded InterReg program linking Strasbourg with Freiburg and Basel.

Assessment of the strategy and 5-year project:

The unit presents an **excellent 5 year research program** with very original and relevant projects that are highly competitive. The major strength is a comprehensive implementation of key technologies, expertise and models that have been established by the laboratory, including access to a high throughput screening platforms, clinically relevant animal models and patient cohorts. Combined with well documented cooperations with other world leading laboratories, the unit provides a **highly integrated unique and powerful center of translational HCV research**, which will be further developing within the future. The excellent infrastructure and a very strong governance with outstanding fund raising (>10 Mio €, including long term funding) and consistent allocation of human resources and budget for consumables and equipment are further keys to excellent future perspectives of this unit.



The scientific research program primarily aims to **study virus host interactions and to develop innovative medicines** for HCV targeting viral entry in a translational research effort. Preliminary unpublished work in animal models suggests that this strategy is effective in combination with other drugs developed by the pharmaceutical industry targeting different steps of the viral life. The program follows 6 axes:

1) Virus - host interactions (viral entry) : Recent findings of the unit showed that SR-B1, CD81, CLDN1 but also EGFR and EphA2 are host factors for hepatitis C virus entry. The importance of these findings is well illustrated by a number of high ranking papers, including *Hepatology* and *Nature Medicine*. The group will analyse the underlying signal cascades. Genome-wide analysis of protein kinases involved in entry already showed multiple hits, which is in agreement with findings on other viruses. Logically the unit proposes a research project, which allows to identify the order and the molecular interactions of the complex pathway. Such analyses will shed light on specific fundamental processes of HCV. Very probably the results will be of high interest not only for this particular virus but also on the entry of other pathogens entering the cell by similar mechanisms. Moreover, this research project has an additional strong translational element in that protein kinases specific for HCV will be used as drug targets. The elaborated techniques and systems present in the unit will strongly support the success of the project. Eventual risks in the finding of successfully applicable drugs are perfectly counter-balanced by the strong impact of the fundamental part.

2) The role of lipoproteins in HCV life cycle. Assembly of infectious HCV virions is still poorly understood, since efficient model systems have been available for a short time only. The unit recently identified an important link between viral proteins and the lipid metabolism network of the host cell by showing that apolipoprotein E (apoE) interacts with the viral nonstructural protein NS5A. The future research aims are directed towards an understanding of the mechanistic role of apoE in the viral life cycle. The unit has established a cell line devoid of apoE expression, which is permissive for HCV entry and replication but impaired in virion production. By expression of distinct apoE mutants this important tool will allow a functional characterization of apoE in viral assembly. Complementary to this approach, the unit has defined certain parts of apoE involved in entry, particularly the heparan sulfate binding domain (HSPG), which might allow the development of inhibition strategies based on HSPG mimetic peptides. This work is funded by LabEx HEPSYS, ANRS and two PhD fellowships from ANRS and MRT and will clearly deliver important novel insights into the functional role of apoE in HCV replication. Furthermore it has the potential to identify novel antiviral strategies targeting entry, assembly and release. Virions with defined apoE mutant will also allow to address functions of lipoproteins in evasion from B-cell responses.

3) Viral evasion and liver disease. Mechanisms involved in the establishment of viral persistence and underlying viral pathogenesis are still ill defined. Previous work of the unit already unraveled the role of viral escape to neutralizing antibody responses and the complex contribution of innate and adaptive immune responses to protective immunity against HCV. The future aims of this project are directed to a better understanding of counterregulatory mechanisms engaged by HCV to evade functional immune responses, to gain closer insights into viral persistence and pathogenesis. This work will be focused on HCV neutralization and evasion from B cell responses by uncovering viral epitopes and entry factor domains targeted by antibodies. The unit will also investigate the impact of lipoproteins in evasion from B cell responses by testing apoE mutants and implement screening approaches to identify common host factors of antibody-mediated neutralization. A complementing approach will decipher counterregulatory mechanisms restraining HCV-specific cellular immune responses, particularly addressing indoleamine 2,3-dioxygenase (IDO), a host gene which is upregulated in acute and chronic HCV infection. The project aims to investigate the molecular mechanism of IDO induction in HCV infection and its impact on HCV clearance and antiviral T-cell response by siRNA mediated silencing and overexpression of regulatory molecules of known IDO pathways. The research plan on viral evasion and liver disease is well feasible and embedded in top-level international research networks receiving funding from ERC and Hepato-Regio-Net.

4) HCV-HIV coinfection. Co-infections with HCV and HIV are common, particularly among injection drug users. HIV elite controllers seem to better control HCV infection as well, in part due to stronger T-cell responses. The project aims to unravel the additional contribution of neutralizing antibody responses against HCV. By taking advantage of a unique cohort of HIV elite controllers, anti-HCV antibodies will be analyzed in HCV co-infected patients compared to HIV progressors and HCV monoinfected individuals. If improved HCV specific antibody response is associated to a better control of HCV infection epitope specificity and subtypes will be determined, as well as phenotypic distribution of B cell subpopulations. The project furthermore aims to gain insights into mechanisms of HCV/HIV immunopathogenesis by correlating humoral immune responses against HCV with outcome of infection and disease progression. The work is supported by funding from ANRS, API Hopitaux Universitaires de Strasbourg, Eurorise, LabEx VRI and Euronet-41. The project follows a clearly defined strategy and could lead to development of immunotherapeutic approaches allowing control of HCV infection and/or delaying progression of liver disease.



5) Development of immune competent mouse models for HCV infection. Such a model would represent a major breakthrough in HCV research and would have a strong impact on our understanding of HCV pathogenesis, studies on immune evasion, vaccine development and provide perspectives to study co-infections of HCV with HBV or HIV. The unit has already established the current state of the art immune deficient mouse model based on uPA SCID mice reconstituted with primary human hepatocytes, allowing to study virus entry, replication and drug development. One strategy of the research program aims to reconstitute a human immune system in this model by transplanting CD34+ hematopoietic stem cells. An alternative approach aims to generate transgenic mice susceptible to HCV infection. Currently the determinants of HCV entry into mouse cells are well understood and transgenic mice expressing human entry factors are in development. However, some host factors required for efficient viral RNA replication seem to be missing in mouse cells and the project aims to identify such factors by library screening approaches in mouse cells. Both approaches involve collaborations with other internationally leading laboratories and are funded by grants from ERC, Investissements d'Avenir, ANR and ANRS.

6) Translational medicine with clinical trials and pathogenesis studies. A major strength of the unit is the availability of patient cohorts and research platforms allowing a streamlined transfer of research data into translational approaches. All of the above projects will generate data and approaches either leading to potential novel antiviral strategies or addressing virus-host interactions involved in pathogenesis, both contributing to the translation research pipeline of the unit. Hallmarks of the translational approach are the identification of key mechanisms of liver graft infection and viral persistence and investigations on the clinical impact of virus-host interactions for liver disease. This approach involves unique and huge patient cohorts available through clinical partners and research networks and is supported by the ERC and EuroNet-41. A second translational effort is aiming to develop first-in-class viral entry inhibitors and vaccines for prevention and treatment of HCV. Most advanced is an investor-initiated clinical trial on the HCV inhibitor Erlotinib starting in 2012/2013, funded by industrial partners and Inserm. This approach is a direct spin-off from the basic research of the unit, demonstrating the comprehensive and interdependent overall strategy. Further mid- and long-term clinical projects are based on the inhibition of HCV entry using monoclonal anti-receptor antibodies, which have been very efficient in a small animal model. Although development of anti-HCV therapies is highly competitive and therefore these projects are risky, the implementation of these research programs will strengthen the visibility and clinical impact of the unit and pave the road for new long term projects, probably focusing also on alternative pathogens and diseases.

Overall the research program is very consistent with complementary approaches from cutting-edge basic science to translational research and clinical trials. Projects and scientists within the unit are highly interdependent providing a synergistic research group.

Some projects are risky, particularly due to the high competition in the research area. The efforts on drug discovery are facing a high competition for HCV drug development driven by the pharmaceutical industry. The inhibitors of viral entry could be used in combination with other drugs developed by the pharma industry which are targeting other steps of the viral life cycle. The innovative nature of the approaches will also provide new and cutting-edge information on HCV pathogenesis and develop into new models to perform translational research. In case of success this approach will be highly beneficial, particularly for patients who are difficult to treat like those suffering from cirrhosis and treatment experienced patients. Development of immunocompetent small animal models is also highly competitive and competing laboratories might be faster. Still, the need for such a model to understand antiviral immune responses and pathogenesis clearly justifies the risk, particularly due to the huge number of potential applications. Overall, the risk-taking is fully appropriate and warranted by the high impact of research results in case of success. The research program furthermore includes a number of excellent and relatively safe projects building on extensive preliminary work, like the further characterization of signaling events upon viral entry, which will help to backup failures to achieve the ambitious goals.

Of particular importance for the translational efforts of the unit is the recruitment of an excellent clinical hepatologist to replace the current head of the hepatogastroenterology department who will retire in 2 years.



Assessment of the unit's involvement in training:

The unit participated very well in the training of students and postdocs on different levels. From 2007 to 2011 27 Master 1, 14 Master 2 were trained in the unit. Seven PhD students and 2 MD students passed their thesis, in addition to 4 "habilitations à diriger des recherches". All students were 100% financed by different sources including the French Minister of higher education but also by 3rd party money. Advancement of the theses is verified by mid-term reviews; the maximal duration of PhD thesis was 3.5 years. The students are represented in the unit's "conseil de laboratoire" and participate in the design and analysis of unit's projects. All students have a permanent partner on the level of the lab and - if required - daily access to the PI. They participate at weekly meeting on the unit level but also on thematic group meetings. The students communicate their results on all levels including international conferences. They further participate in meeting organizations, including the annual Biotechnology forum of Strasbourg. The good career development strategy of the unit is documented by the positions of the students after finishing their thesis, which comprises high-level academic institutions as Stanford and Harvard Medical School, University of Pennsylvania but also in industry (Gilead, Nycomed, Covance, Biomérieux).

The members of the unit participate in graduate education in Master and PhD programs of the local graduate school as well as on different levels of medical education (DCEM 2, 3, 4). Remarkably, postgraduate training is realized not only on the local level (postgraduate courses in virology in liver disease) but also on the European level (EU Europrise, EASL).



4 • Grading

Once the visits for the 2011-2012 evaluation campaign had been completed, the chairpersons of the expert committees, who met per disciplinary group, proceeded to attribute a score to the research units in their group (and, when necessary, for these units' in-house teams).

This score (A+, A, B, C) concerned each of the four criteria defined by the AERES and was given along with an overall assessment.

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

❖ Overall assessment of the unit :

Virus-host interactions and liver disease

Excellente unité à tous points de vue.

Grading table:

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



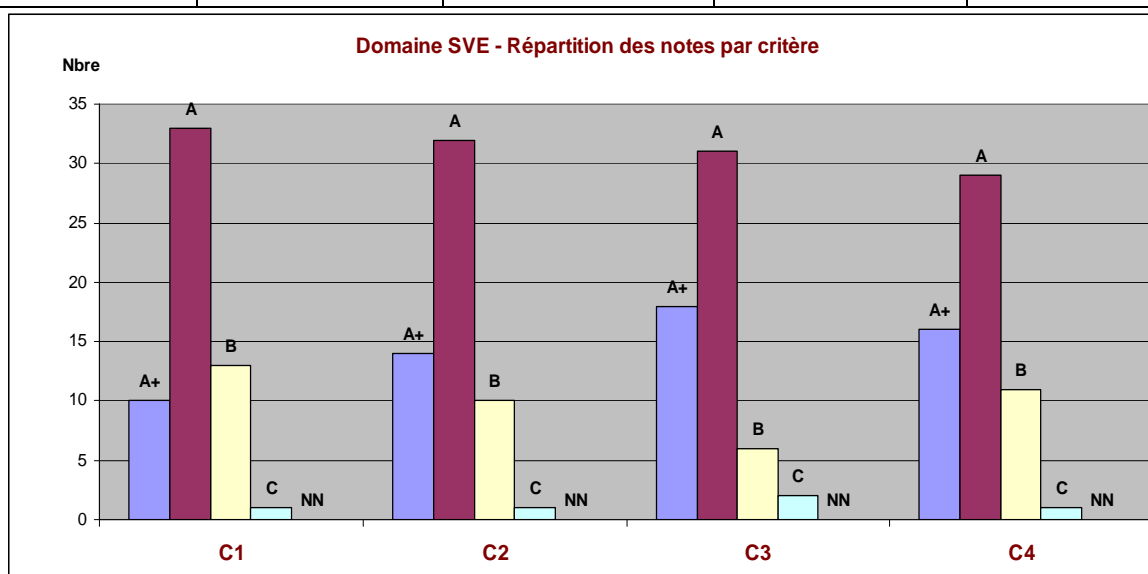
5 • Statistics per field : SVE au 10/05/2012

Notes

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

Pourcentages

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





6 • Supervising bodies' general comments

Monsieur Pierre GLORIEUX
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Alain BERETZ
Président

Strasbourg, le 28 février 2012

Objet : Rapport d'évaluation de l'UMR_S748 (réf. S2PUR130004543)
Réf. : AB/EW/N° 2012-80

Direction de la Recherche

Cher collègue,

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Je vous remercie pour l'évaluation de l'unité de recherche «Interactions virus-hôte et maladies hépatiques» (IVH – UMR_S 748) dirigée par Monsieur Thomas Baumert.

Vous trouverez ci-joint les réponses du directeur d'unité de recherche concernant les erreurs factuelles et les remarques et appréciations du comité d'experts.

Je vous prie d'agréer, Cher Collègue, l'expression de mes sentiments distingués.


Alain BERETZ
Président



P.J. :

- Une première partie corrigeant les erreurs factuelles
- Une seconde partie comprenant les observations de portée générale

Strasbourg, 23 February, 2012

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**Response to the AERES report regarding unit UMR_S748
“Virus-host interactions and liver disease”**

Thomas Baumert
Directeur
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Praticien hospitalier
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Reference: C2013-EV-0673021V-S2PUR130004543-RT_BAUMERT.pdf

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In the name of the collaborators, members and clinical partners of Inserm unit UMR_S748, I would like to thank the AERES visiting committee for the site visit. We acknowledge the thorough and detailed evaluation and appreciate the very positive comments of the committee.

We are aware that it is of particular importance for the clinical unit program to recruit a clinical hepatologist to replace the current head of the Hepatology-Gastroenterology service at the Strasbourg University Hospital who will retire in 2014. We would like to inform the AERES that the preparation of the recruitment through the Faculty of Medicine of the University of Strasbourg is ongoing.



**Professor Thomas Baumert, MD
Head, Inserm unit UMR_S748**