CIML - Centre d'immunologie de Marseille - Luminy

Rapport Hcéres

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

Section des Unités de recherche

AERES report on the research unit

Center of Immunology Marseille-Luminy

From the

University of Marseille-Luminy

March 2011

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Le Président de l'AERES

Didier Houssin

Section des unités de recherche

Le Directeur

Pierre Glorieux

March 2011

Research Unit

Name of the research unit: Center of Immunology Marseille-Luminy (CIML)

Requested label: UMR_S INSERM, UMRCNRS

N° in the case of renewal: UMR_S631, UMR6102

Name of the director: M. Eric VIVIER

Members of the review committee

Committee chairman

M. Jean-Claude WEILL, Institut Necker, Paris, France

Other committee members

M. Philippe BOUSSO, Institut Pasteur, Paris, France

M. Adrian HAYDAY, London Research Institute Cancer Research London, UK

M. Bruno LEMAITRE, EPFL, Lausanne, Switzerland

M. Markus MANZ, University of Zürich Medical School, Zürich, Switzerland

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Report

1 • Introduction

- **Date and execution of the visit**

The site visit of the UMR Inserm U631 took place over three days from March 15th-17th , 2011. The organization allowed the visit to go very smoothly. The visit started by an overall presentation of the global structure and scientific goals by the Director, Dr. Eric VIVIER. Then, each team had 45min (20min presentation and 25min discussion) to describe their achievements and projects. The committee had enough time to listen to the presentations, discuss their scientific content and to evaluate the research of each of the 18 Teams (2006-2009 report). Further, the committee had a chance to meet and discuss quite in-depth with each staff category. In addition, discussions with researcher and students around their posters and in a more informal manner could take place.

At the end of the visit, the review panel met to exchange their views and to organize the preparation of the final report.

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

The CIML is dedicated to the study of Immunology from minor organisms to humans. Research is transversal and multi-disciplinary.

It was created in 1977 and includes today more than 200 researchers as indicated in the table below. It is hold in an entire building in the Marseille-Luminy Campus. It includes 18 research teams of variable size as well as 17 platforms.

- **Management team**

The CIML is a unique place to do research thanks to its exceptional scientific environment, its democratic management and the excellence of its teams, including the managing and administrative one. Overall, we felt that the center is very well managed. More specific comments are included below.

The scientific strategy of the CIML is clever and clear: (1) recruitment of new lab-heads based essentially on the originality and talent of the candidates and (2) development of potent technical platforms in order to provide the best support for the teams of the center.

- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	10	10
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	43	46
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	37	37
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	63	63
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	28	28
N6: Number of Ph.D. students (Form 2.7 of the application file)	36	32
N7: Number of staff members with a HDR or a similar grade	28	28

2 • Overall appreciation on the research unit

- **Summary**

The site visit lasted two and a half days. We listened to 18 talks by the different group leaders. This visit was concomitant to the visit by the CIML international Scientific Advisory Board (SAB), creating an opened and constructive atmosphere of discussion between all of us.

There were four talk sessions. We had a debriefing meeting to summarize together with the SAB our opinions on each team talk and projects at the end of each session. The general impression was excellent thanks to the outstanding quality of the science presented (reports and projects) and to the passion for science that was in the air and could be felt by all of us.

The poster sessions during lunches and prior to dinners were also very animated in terms of scientific communication and exchanges.

The discussions during the private meeting between the committee and researchers, post-docs, students and technical staff were very fruitful and could help the committee identify some specific points that were ultimately shared with the CIML director.

In the overall, we all felt that the CIML is an excellent research center from all point of views.

- **Strengths and opportunities**

The CIML is “a big but not too big” research center, as underlined by the director. The committee thinks that it should remain this way. Indeed, because of its reasonable size, the CIML teams can productively collaborate together and share technics that obviously, due to their increased sophistication, cannot be re-invented by each team. Scientists at

the CIML have understood that “what is good for the center is also good for them”. In other words, it is a place where there is a true scientific collective life that makes the research very efficient and the center very attractive.

The recruitment of young gifted group leaders ensures an exciting renewal of the research carried out in the center.

The CIML is made of original individuals with complete freedom of thought. This particular feature of the center should remain the main criteria for selection of new groups and for support for the existing teams.

- ## Weaknesses and threats

The only general weakness that came out from our discussion with researchers, students and technical staff of the CIML was a request for more dialogue with the direction. The committee feels that -given the size of the center- the director should be surrounded by 4-5 group leaders who can meet regularly in order to tackle the different problems when they come out. Indeed, flexibility is key for such a big structure full of talented people to work efficiently. This decision group should be in a good position to handle and to communicate key issues related to the management of the center, such as:

* To be able to reinforce one group that is -at a given moment- on a very hot finding.

* To contribute with technical (or other) help to some of the platforms, in order to avoid that the scientist who has set it up becomes “a servant” for his colleagues at the expenses of his own research.

* To discuss with group leaders sensitive political issues such as signature problems for CR1 who supervise a project and may need a senior authorship to progress in their career.

* To encourage meetings between students and post-docs to promote the exchange of ideas and techniques.

All these issues are not unique to the CIML: they are the classical ones in all French research environments but the CIML -due to its ideal size and its mode of governance- has the capacity to solve them more easily. So they should take this opportunity.

- ## Recommendations to the head of the research unit

* To give -if possible- to the laboratories that have built a scientific platform the technical support they need so that they can properly transfer their knowhow to their colleagues without seeing their own research affected.

* To elaborate precise rules for the replacement of available space after the departure of team taking into account the promotion of inside researchers as group leaders.

* To accompany the closing of Ms. SCHMITT-VERHULST’s team that has very exciting results on the molecular bases for T lymphocyte function in melanoma by helping her to transfer her animal models and the scientists associated to her team to other(s) groups in the center. Indeed, we felt that it would be deleterious for the CIML to loose this research line.

* On the same line, to make sure that the research on B lymphocytes is not lost once Ms. Claudine SCHIFF retires. We thus strongly recommend to the CIML director to actively search for a group leader working in the B cell field.

* To provide the proper help to Ms. Lena ALEXOPOULOU for her to reinforce her team that has suffered a dramatic reduction in size. We also recommend to the CIML director to encourage her to focus her research on the projects for which she can be at the forefront.

* To continue keeping the group leaders happy.

* To reinforce the PhD program that was recently created.

- **Production results**

A1: Number of permanent researchers with teaching duties (recorded in N1) who are active in research	9
A2: Number of permanent researchers without teaching duties (recorded in N2) who are active in research	39
A3: Ratio of members who are active in research among staff members [(A1 + A2)/(N1 + N2)]	0.91
A4: Number of HDR granted during the past 4 years	8
A5: Number of PhD granted during the past 4 years	39

3 • Specific appreciation on the research unit

The CIML is without doubt one of the best immunology centers of excellence in Europe. It comprises 54 scientists, 93 engineers and technicians, 36 post-doctoral fellows and 40 M2-PhD students. The list of publications that has been produced during the last five years is impressive with 234 articles published, among which 78 have appeared in top-ranked journals. Most group leaders are regularly invited to international meetings and are awarded peer-reviewed project-based grants. The variety of topics around a central theme and the diversity of individuals make the CIML a unique place in which a C. elegans expert can work but also an Emmerit Professor who pursues his life-long quest on the mechanism of cellular death by using a protist (Dictyostelium) and who at the same time shares with his younger colleagues his intellectual, curiosity-driven approach to science. The committee felt that maintenance of such diversity is the key for the success of the CIML.

4 • Appreciation team by team

- **Team name: "Toll-like receptors in Immunity"**
- **Team leader: Ms. Lena ALEXOPOULOU**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)		0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	0
N7: Number of staff members with a HDR or a similar grade	1	1

- **Appreciation on the results**

This team focused its activity on deciphering the contribution of different innate immune sensors (Toll-like receptors or TLR) in infections and autoimmunity. The team is exploring this network of pathogen-recognition systems using TLR- deficient mice exposed to different pathological conditions. Eventhough, this might appear as a conventional approach, the group has been seeking for specific "niches" as the forsaken murine TLR-8 and combinatorial TLR interplay.

The team largely contributed to the better understanding of the TLR interplay in immunopathologies. The team has been working at the leading edge of the field showing (1) the involvement of TLR-5 in the recognition of flagellated bacteria (PNAS 2006), (2) that the supposedly inactive murine TLR8 was actually involved in autoimmunity (J Clin Invest 2010), (3) the respective contribution of TLR-7 and 9 in autoimmune myocarditis (Autoimmunity 2010). They also collaborated with local, national and international groups on the role of TLR in viral (J.immunol 2008 and 2009) and bacterial (Plos. Pathoge 2008 and 2010) infections.

The team has been involved in 25 original publications with Dr Alexopoulou signing as first author (Eur. J. Immunol. 2006 IF~4.5), last author (PNAS 2006, J Clin Invest 2010 IF~16.5, Autoimmunity 2010 IF~2.5) and contributing author to the 20 others works. The team leader is well recognized and the number of collaborative works clearly indicates her international expertise.

The team has been extremely attractive and was composed at least of a couple of postdoc and PhD students (5 postdoctoral fellows and three PhD students). However, since 2008, the team progressively lost attractivity and most

of the partners left the lab. The team is actually composed of a research assistant and an assistant professor. It seems that the team is actually undersized and may not be able to reach their goals.

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

The team has been highly involved in the TLR field with more than 80 % of Dr ALEXOPOULOU's published work performed in collaboration, approximately 20 % with local, 10% with national and 70% with international groups.

The team was suceefull in raising funds with competitive fundings such ANR (2007-2010) and a contract with Innate pharma (2006-2009). However, since 2008, no grant has been received by the team and this may jeopardize the future of the team. In addition, no postdoctoral position has been secured for the future.

The team is clearly collborating with a large number of local, national and international colleagues in the field of TLR. However, the comittee regrets that most of the works are not co-signed in leading position.

The team is actually reduced to its lower limit with one research assistant and one assistant professor. It would be important to distinguish if the small size of the actual team is transient due to personal issues (The PI have two babies in last years) and current difficulties in the scientific project (deciphering the function of TLR8 was more complicated than expected) or reflect a lack of charisma of the PI and/or a lack of interaction with the CIML and other partner institutions.

- **Appreciation on the project**

The team is proposing a large program on TLR localized in the endolysosomal compartments. The program will :

- dissect mechanisms by which TLR7/8/9 contribute to the development of systemic lupus erythematosus; this will be investigated in mice using TLR-deficient mice and in human by genetic associations and functional studies. Recent results indicate that TLR8-deficient mice spontaneously developed glomerulonephritis while TLR8/7-deficient mice were protected indicating interplay between these two TLRs. In addition, TLR9 deficiency also lead to TLR7 overexpression. How TLR interact will also be studied in Lupus patients by correlating TLR polymorphism and monocyte/DC functions. The committee felt that the program need to be better define and lack in depth focus.

- explore contributions of TLR8 in viral infections; surprisingly, the viral models to test are not selected yet because the team wants first to address in vitro relevance of TLR7/8/9. We might argue that this in vitro approach may biased in vivo investigations.

Role of TLR signaling in B1 cell : this aspect has never been studied yet and may be very attractive.

The committee appreciated the ambition of this program to tackle TLR interplay in disease settings as diverse as autoimmunity and viral infections. The committee felt also some inadequacy between the size of the group, the funding and the breadth of the program. In addition, the program obviously asked unexplored questions but the hypothesis driving the program were not obvious to the committee.

- **Conclusion**

  - Summary

The committee appreciated the tremendous amount of work performed by the team on the understanding of TLR interplay. The work was acknowledged in numerous collaborative works and in a recent publication in J. Clin. Invest (2010).

  - Strengths and opportunities

The tools that generated the team (TLR8, 7/8 and 8/9 deficient mice) are strong assets for the future and the team may want focused on better characterizing the interaction between these molecules in infectious models that are already largely exploited locally.

— Weaknesses and threats

However, the committee felt concerns about the coming years that may be critical for the research program. Indeed, the reduced size of the team and the lack of secure funding appear to be the main limitations in the resurgence of the team. The committee felt some inadequacy between the breadth of the research program (TLR 8 and 9 in human and murine lupus, TLR8 in viral infections and TLR in B1 B cell biology) and the manpower of the team. The committee failed to see clear insights of the hypothesis driving the program and was concerned about models directing the research activity.

— Recommendations

The committee felt concerns about the coming years that may be critical for the research program. It would recommend to seek for more focused and in depth activities. A transition period might be a good opportunity to debate on fundamental questions raised in the TLR field and to delineate programs that would fit CIML strategic views and ambitions. We recommend a discussion between the team leader with the CIML direction to decipher strategies that could reinforce the team and improve its integration at CIML. The expertise of the team leader as well as the topic of the team could clearly be an asset for the CIML if this team is more solid and better integrated.

- **Team name: From lymphoid structure to lymphocyte migration**
- **Team leader: M. Marc BAJENOFF**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0,8	0,8
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	0	0
N7: Number of staff members with a HDR or a similar grade	0	0

- **Appreciation on the results**

The team leader is an outstanding young scientific with tremendous potential. After a landmark paper during his postdoc, he continued to be very productive (3 first author papers in 3 years, Blood, J. Immunol, PlosOne) as he transitioned to a PI position in early 2010. He also wrote 4 reviews. Some of his most recent achievements were therefore performed before starting his own lab. With these seminal publications, the team leader has established using two –photon imaging the critical role of stromal cells and of the lymphoid organs architecture in guiding lymphocyte migration in vivo. Of note, a new two-photon microscope has been set up recently at the CIML and after

only one year, the first paper from his lab has just been published (Journal of Immunology). While it is certainly too early to judge the scientific achievement as a PI, his scientific productivity so far has been excellent.

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

The recruitment of the team leader is a great opportunity for the CIML and several collaborations have already been set-up that should highly benefit from the team leader's expertise in in vivo imaging. As the team has been created recently, the group is still quite small but is expected to grow over the next years. Several sources of funding have been secured already for the next 3 years (ANR JC, INCA, ARC, FRM…). Since 2007, the team leader has participated to six international meetings.

- **Appreciation on the strategy, management and life of the team**

The management of the team appears very good. The committee feels that it is important that the CIML ensure that the team leader has enough manpower to run his own projects and help his/her colleagues interested in intravital imaging technologies.

- **Appreciation on the project**

The project is very clearly outlined and aims at i) understanding the remodeling of the lymph node stroma during inflammation and ii) study T cell motility in solid tumors. The questions are original and very important and the project appears feasible. The team leader will exploit his unique expertise in the field of cell migration in vivo. The team is currently developping a multicolor reporter mouse strain to assess stroma remodelling during infection. This approach is extremelly elegant and illustrate the creativity of the team leader. If successful, the reagents built in the process are expected to be very useful for this and other purposes. It was felt that given his strong potential, team leader should be even more ambitious in his scientific aims in particular in dissecting the mechanisms underlying the phenomenon that he plans to observe. The use of lasermicrodissection to isolate and study LN FRC may face a sensitivity issue.

- **Conclusion**

  - Summary

Very promising team leader with excellent track record and unique expertise at the CIML. The project is very innovative, based on cutting edge approaches and cleverly devised strategy. Additional approaches to manipulate the experimental systems may further strengthen the project. Chances of success are very high.

  - Strengths and opportunities

Clear potential to create synergy with other team at the CIML. Potential to apply the methodology to human samples.

  - Recommendations

It is recommended that the team leader is given enough technical support (in term of personnel) so that collaborations will not distract him from his own research.

- **Team name: ABC transporters in membrane dynamics**
- **Team leader: Ms. Giovanna CHIMINI**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	-
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	-
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	4	-
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	-
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	2	-
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	-
N7: Number of staff members with a HDR or a similar grade	1	-

The team is now closed

- **Appreciation on the results**

The team was a well funded and well establsihed laboratory working on ABC transporters and membrane dynamics. The publication output during the review period was impressive and there is no doubt that the PI has a strong standing in the field. Nevertheless the PI decided to reorient her activities and accepted a CNRS directorship focused on science administration and communication. As a consequence the PI made the wise decision to focus her efforts and the lab is closed. Hence, the report will not focus on the scientific activities.

The team publsihed 25 articles during the review periods, a large proportion last authored by the PI. The publications were in high class journals throughout.

The newly established office is aiming at establishing industrial collaborations, foster international scientific collaborations, and enhancing the international visibility of the institute. Most importantly an international PhD school is established that includes a student exchange program with Harvard Medical School.

The partnership with Harvard Medical School has been successfully established and it is a remarkable achievement that the exchange is two sided and that US students visited Luminy for internships. This is a very important step for the Campus. Also the association with Shanghai is a crucial development as it might open the institute a huge resource of young researchers.

The initiative of the office to foster communication between industry and the institute cannot be valued high enough. As the office is just established results are only expected during the next review period. Relevance of the initiative cannot be evaluated yet, however the sheer fact that an international graduate school is establsihed is of highest importance for the institute.

The establishment of a graduate school fills an important gap at the campus. The lack of international spririt among the students was a clear disadvantage of the institute. This problem will hopefully be successfully tackled by the office.

- ## Conclusion

  - Summary

The PI quits scientific activities after a fruitful time as a researcher in the field of ABC transporters and decided to continue in scientific administration. Responsibilities of the newly founded office are the establishment of industrial and scientific collaborations at the international level as well es establishing an international and interdisciplinary graduate school. The newly established office could be of extreme importance of the institute.

  - Strengths and opportunities

Making the institute a place that is easily accessible to international students will open access to enormous human resources.

  - Weaknesses and threats

Especially the language barrier has to be overcome. It has to be as effortless as possible for a foreign student to establish life in Marseille. It is also crucial that the multidisciplinarity of the institute is reflected in the graduate program. Theoreticians have to be properly embedded and supported both from the immunology perspective but also from their respective discipline.

  - Recommendations

As the office could be of extreme importance for the institute it will be essential to develop it adequately and to hire adequate personnel.

- **Team name: Dendritic cells and anti-viral defense**
- **Team leader: M. Marc DALOD**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	3	3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	0
N7: Number of staff members with a HDR or a similar grade	1	1

- **Appreciation on the results**

The team has been working on 2 major axes: 1)-the roles of dendritic cell (DC) subsets in antiviral defence and their molecular regulation; 2)-the interactions between DC and natural killer cells (NK) in shaping the antiviral CD8 T cell response. Two major DC subsets have been studied: plasmacytoid DC (pDC) and CD8¤ + type DC. The functional characterization of DC subsets is less advanced in human than in the mouse. For this purpose the team has developed an original strategy based on comparative genomics of immune cell subsets between the mouse and the human. This approach has confirmed the strong similarity between mouse and human pDC and led to propose novel hypothesis on their functions. They have identified human BDCA3+ DC as equivalent to mouse CD8¤+ DC and thus likely professional cross-presenting cells. Thus, these cells may be used as target for the development of innovative vaccination strategies against intracellular pathogens. The team has also identified novel genes as candidates for the dissection of the mechanisms regulating DC differentiations and functions Collectively, this body of work has successfully addressed major questions, providing important contributions to the field. The work performed has clear elements of innovation and has followed a logical and coherent path of development.

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

In the past 4 years, the team has published 19 research papers. Among them, the very original work in Journal of Experimental Medicine (2010) about the identification of XCR1 as a novel membrane marker specifically expressed on mouse CD8a +, human BDCA3+ and sheep CD26+ DC. The team leader and one senior post-doc have been invited to deliver lectures at several international meetings and at various institutions in France and abroad. The team has therefore a good international visibility.

- ## Appreciation on the strategy, management and life of the team

The team comprised 1 researcher (CR1, CNRS), 4 post-doc, 1PhD student and 2 Masters. The management of the group appears to be effective, and is facilitated by the relative small size of the team.

Partnerships have been established with several excellent research groups in France.

The team has successfully applied to competitive funding and able to raise funds.

- ## Appreciation on the project

The future plans of the team are articulated in several well-defined projects : (1) Role of pDC in antiviral defense. A first aim is the generation of a mutant mouse strain allowing complete and specific pDC depletion; impact of pDC depletion on antiviral defence; monitoring pDC trafficking during antiviral response, (2) Role of CD8a+ like DC in antiviral defence. Role of XCR1 in the cross-talk between CD8a+DC and NK or CD8 T cells; generation of mutant strain depleted of this subset, (3) Extension of the studies to human DC. The committee has proposed to give the priority to this last perspective and to elaborate with humanized mice.

A very original topic is concentrated around the evolution of DC subsets through comparative immunology.

These projects integrate very well with other projects at the CIML and will contribute to its success.

- ## Conclusion and Recommendations

The committee was very satisfied by the program and the clear formulation of the future projects. With the addition of a novel researcher, the team will be able to sustain competition in the field.

- **Team name: Innate Immunity in C. elegans**
- **Team leader: M. Jonathan EWBANK**
- **Staff members**

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

- **Appreciation on the results**

This team is one of the 2-3 best teams world-wide working on C. elegans immunity and more globally one of the top C. elegans teams in Europe. In the last years, the team has developped several models of infection and obtained important results on C. elegans host defense. They have i) characterized several pathways regulating the host defence of C. elegans, ii) identified the first antimicrobial peptides of C. elegans, iii) developped a model of natural infection of C. elegans with a fungus, iv) discovered a paracrine mode of regulation of antimicrobial peptides that involved neurons … The number of publications in high impact journals (Nature Immunol, Cell Host and Microbes, Current Biol…) is very high. Team leader has been invited to many meetings, wrote comments and reviews and as a consequence, benefits from a high visibility in the field of innate immunity, host-pathogen interactions and evolution. This team participates to the high reputation of the CIML.

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

The team has established several important collaboration in the last years. They have developped a high throughput screening facility at Marseille and been actively involved in the development of genomics platforms in the Marseille area. His laboratory masters a large spectrum of methods and is a reference laboratory for C. elegans high-throughput screens. This team has been very well funded (ANR, FRM équipe).

- **Appreciation on the strategy, management and life of the team**

Team head is clearly a charismatic leader developing cutting-edge and ambitious projects. With a strong expertise in the fields of transcriptomics and high-throughput genetic screens, he actively contributes to the structuration of the research at the regional and national level. His team is solid and includes now 6 scientists with a permanent position.

- **Appreciation on the project**

The project of the team is to carry out a « systems based approach » of the C. elegans epidermis response upon infection with the nematophagous fungus Drechmeria conidia. This includes high-throughput genetic screens (RNAi, EMS) using reporter genes of antimicrobial peptides as a readout and several biochemical screens (TAP-TAG, Yeast 1 hybrid, DNA Chip). These approaches should provide a detailed view of the pathways activated by this fungus. This team has mastered many of the techniques required for this systems biology study and participated in the development of new tools. Expected results are the precise delineation of pathways activated during the immune response, analysis of the cross-talk between injury, stress and host defense pathways and possible cross-talk between physiology and immune responses. These projects are in line with a recent shift in the field of innate immunity that aims to analyze the host reponse to pathogens from a more global perspective.

- **Conclusion**

— Summary

The project is clearly outlined and includes the development of systems-based approaches. The team is one of the most solid and most renowned teams of the CIML. The size of the team is considerable and includes several permanent position scientists. This should facilitate the integration of several high-technology approaches within the laboratory. Team leader is also a very open-minded scientist that participates in the scientific life of the CIML.

— Strengths and opportunities

* The originality of the C. elegans model of host defense with genomic and genetic tools.
* The high reputation of the team with an impressive record of publications.
* The solidity and stability of the team that masters a large spectrum of techniques.
* This team also brings a strong expertise in genomics and genetics to the CIML and is well integrated.

— Weaknesses and threats

The systems biology approaches described has the drawback of large-scale approaches lacking specific questions.

The C. elegans immune response appears quite different from that observed in vertebrates.

— Recommendations

The team should be strongly supported. It is important that this team continue his original exploration of the C. elegans host defence response with all the freedom required. It is possible that the most interesting question in this system differs from traditional immunology. There is also a need to better define the scientific questions underlying the large-scale systems based analysis. The size of the team should allow the development of ambitious systems-based projects but leave space for exploratory research.

- **Team name: Lymphoid cell differentiation and the control of gene expression and recombination**
- **Team leader: M. Pierre FERRIER**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	3	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	0
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	6	4
N6: Number of Ph.D. students (Form 2.7 of the application file)	7	6
N7: Number of staff members with a HDR or a similar grade	2	2

- **Appreciation on the results**

The team leader has a long-established reputation in the investigation of gene expression and gene rearrangement dynamics in lymphocyte development. Indeed, the lab has been at the leading-edge of how an enhancer element may separately yet co-ordinately regulate gene rearrangement and expression. Over the past review period, the team has collaborated with a lab at Washington U which has resulted in several papers in journals such as Immunity and Nature Immunology. The lab's interests have pushed it to pursue, to develop, and to import into the CIML several state-of-the-art, high-throughput techniques in defining the interactions of specific proteins with chromatin at key gene- and locus- regulatory sites. This in large part followed from the team leader sabbatical leave, and the team leader is now supervisor of the new bio-informatics platform at CIML. These approaches have been applied to the regulation of gene expression programmes in transformed cells as well as normal cells, and the lab has established an effective collaboration with oncologists so as to obtain and understand clinical samples. Aware of the complexity of the data that emerge from these types of studies, Dr FERRIER has also established effective collaboration with mathematical modelers, with one benefit being a revised model for the regulation of allelic exclusion, a key but poorly understood component of adaptive immune responses. The lab has also made individual progress in its component of the heavily-delayed international Regulome project, focusing on the ubiquitous co-activator Mediator complex, Med1. Overall, this is an established lab whose impact may grow substantially with their mastery and application of new epigenetic methods.

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

The team leader is highly active, making recognized contributions on many aspects of lymphocyte development and gene regulation; has participated in many international meetings; and more recently has been called upon to organize international conferences on chromatin and epigenetics. He is involved in many international collaborations including

the multi-centre Regulome Project to understand the mechanisms by which key transcription and chromatin factors work in vivo. The lab has hosted 7 PhD students and 3 postdocs over the review period, together with several other researchers and engineers. It is an highly interactive lab, with key collaborations with clinicians, with other molecular biologists and with the Centre for Theoretical Physics, Luminy.

- **Appreciation on the strategy, management and life of the team**

The Lab Head has a clear vision for the development and application of high throughput genomics technologies. This is excellent, although it might be argued that the quality and impact of the lab's publications might be improved if their own application of their technologies was focussed on fewer goals. The lab has been successful in attracting strong, external, peer-reviewed grant support. The team benefits greatly from several senior scientists although it appears to lack a permanent technician devoted to "wet lab" research. This issue deserves consideration.

- **Appreciation on the project**

The team's import into CIML of multiple high throughput genomics techniques, coupled with expertise (via collaboration) in mathematical modeling and complex data handling is an exciting development. The proposal to examine in parallel patterns of normal and malignant development is likewise important, and resonates with the goal of increased translational research articulated by the CIML Director. However, it will be absolutely critical for the CIML to establish a clear structure by which the application of the new techniques to the team research projects is not hindered by pressure to apply the techniques to multiple labs via some form of core facility for which the team leader would appropriately serve as academic director. The lab's application of the new techniques should be focused so as to incrementally build substantive studies in key areas of lymphocyte development and lymphomagenesis. The group may need to de-emphasise some commitments, such as the Regulome project. The project on long-range interacting forces is ambitious but via in-house expertise and collaboration the lab is well-placed to attempt this worthwhile endeavour.

- **Conclusion**

  - Summary

The team leader is an accomplished and well-regarded basic scientist, with an outstanding capacity to develop effective collaborations with a broad range of investigators. The CIML can benefit immensely from the team's expertise. There may be too many projects proposed, and a re-evaluation may result in a better balance of important, solid studies of gene and chromatin regulation together with more speculative investigations involving highly sophisticated modeling that may be very incisive.

  - Strengths and opportunities

State-of-the-art genomics expertise with a skill and commitment to continue the development of these techniques. Many studies of the interactions of chromatin with important transcription factors suffer from the poor quality of antibodies against those factors. The successful antibody derivation facility at CIML offers the chance to obtain new antibodies that could be applied locally in ground-breaking studies, and might additionally aid the community. The lab comfortably spans clinical investigations and high level mathematical modeling and the analysis of complexity.

  - Weaknesses and threats

The understandable interest of the CIML in having the team leader supervise a genomics /epigenetics core facility and centre for expertise must not be realized at the cost of the team leader's research programme. Th team leader lists an aspiration to improve the impact of the publication record, and this is likely to be threatened without some improved focusing of the research goals. Contribution to projects such as the Regulome might need to be re-evaluated. The ENU approach is currently a great opportunity for the lab. It requires a high investment, important resources and optimal screening strategies but is compensated by its upward potential. The decision on whether to extend or reduce such program will require the overall output to be evaluated in a few years.

- **Team name: Molecular bases of programmed cell death**
- **Team leader: M. Pierre GOLSTEIN**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	0
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	0	0
N7: Number of staff members with a HDR or a similar grade	1	1

- **Appreciation on the results**

This group uses Dictyostelium to determine the molecular mechanisms that underlie the determination of autophagic cell death. The PI was a well-known Scientist in the field of cell death. Over the last 15 years, taking advantage of his status of Emeritus (after retirement), the PI developed Dictyostelium as a new model to study specific types of cell death. This new project has been quite productive: 19 primary research publications in good impact journals (Embo Report, Mol. Biol. Cell, Autophagy, Cell Death Diff), several reviews and three book chapters. Overall, the team leader's track record is very good in this "new life".

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

As mentioned previously, the PI was internationally very well known in the field of cell death. During the last period, the team consisted in one technician, a post-doctoral fellow and two PhD students who have successfully defended their thesis. For the next period, the team is dwindling in numbers and space, with only the technician left. However several students will help during short-term stays. The PI has obtained funding from several sources, including ANR, ARC, Research Ministry and La Ligue contre le cancer. The group's visibility is high with many invitations to speak at international meetings.

- **Appreciation on the project**

The team leader proposes to follow on his project, which is clearly conceptually innovative. Today, there are several forms of cell death that are clearly recognized: necrosis, apoptosis, but also pyroptosis and autophagic cell death (ACD). In order to understand the later, and to use genetics to unravel the molecular details of this kind of cell death, the PI used Dictyostelium, a rather less known model organism but clearly well adapted to the project. Briefly, a random mutagenesis screen has identified several mutants critical for ACD. The genes responsible for these mutations

have been isolated and a tentative pathway has been defined. The project aims now at completing this pathway and understanding the relationships between the players at the molecular level, using proteomics and again genetics. The approaches are straightforward and well focused. The project is interesting and the PI's expertise together with the use of an excellent model system, predict success.

- **Conclusion**

  - Summary

The project is clearly outlined, with solid background and creative prospects. The team leader is considered as an "historical" outstanding asset to the CIML and will be successful in reaching the goals proposed during the next 4 years. Considering the size of the team and the space allocated, the quality/price ratio of the project is outstanding. Finally the PI has a very special situation in CIML. His vast experience, knowledge and intellectual resources are readily available to any student or young scientist in need of advice as his door is always open and he enjoys discussing and mentoring.

  - Strengths and opportunities

Original model of cell death with genetics.

  - Weaknesses and threats

The Dyctiostelium model is not widely known and ACD, when deciphered in this model, perhaps not directly transposable to vertebrates.

  - Recommendations

This project is an added value to CIML nearly for free except if space becomes an issue for the development of other teams.

- **Team name: Immunology and cell biology of pathogen/host cell interactions**
- **Team leader: M. Jean-Pierre GORVEL**
- **Staff members**

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

- **Appreciation on the results**

This group is devoted to infection and studies host-pathogen interactions, focusing on three pathogens: Brucella, Salmonella and more recently Mycobacterium. They showed that Brucella replicates in the endoplasmic reticulum of dendritic cells, which allowed them to establish that this bacterium controls immune recognition via its LPS (shield against the TLR4 pathway). A specific new class of molecules, Brucella Toll-like interacting protein (Btp) controls the TLR pathway. They found also that Brucella beta-cyclic glucan can be used as an adjuvant. They analyzed the maturation of the Salmonella-containing vacuole and found that the type III Secretion System effectors PipB2, SopD2 and SifA control the recruitment of kinesin-1 to the vacuole. Finally, they have shown that cholesterol is essential in maintaining the tight apposition of the vacuolar membrane with arrested Mycobacterium. This bacterium accumulates lipid inclusions as energy storage and induces the differentiation of foamy macrophages. This team has been extremely productive: 43 primary research publications in high impact journals (Science, PNAS, PLOS Pathogen, JIM), four excellent reviews (Nature reviews series) and two book chapters. Overall, the team leader's track record is outstanding.

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

The PI is an international figure in the field of host-pathogen interaction. During the last period, the team consisted in 5,5 permanent researchers at Inserm, CNRS or University, 4 technicians, one post-doctoral fellow and 2 students. For the next period, the team plans to recruit 2 new students and a post-doc, which is necessary in order to improve the balance between students and permanent positions. The funding is truly impressive with more than 20 contracts (10 ANR!). The group's visibility is very high with editorial duties and many invitations to speak at international meetings. The project on adjuvant and DCs of has led to an integrated collaboration of the PI with the Baylor Institute of Immunology Research (BIIR) in Dallas (USA), where he will spend part of his time over the next period. Several excellent senior scientists will take care of the team and the second translational collaboration that has been set up locally with Marseille.

- **Appreciation on the project**

The team has outlined projects clearly based on and emerging from previous work in host-pathogen interactions. The project is original, based on several findings of the preceding period and follows roughly the direction of the three models (Salmonella, Brucella and Mycobacterium). Interestingly, the host part (DCs, adjuvants and vaccination) is taking a bigger part in the project. The translational collaborations with the University de la Méditerrannée (Marseille) and BIIR (Dallas, USA) are extremely well timed.

- **Conclusion**

  - Summary

Highly promising project based on excellent past work with documented achievements record and highly productive research group with solid local, national and international collaborations.

Clear prospects, with strong hypotheses but creative and cutting-edge research.

Excellent prognosis on fulfilling the research goals through the upcoming 4 years of funding.

  - Strengths and opportunities

Excellent basic science with strong translational output in a well-integrated team.

  - Weaknesses and threats

Lab. management might be difficult if the PI spends an important part of his time in the BIIR.

  - Recommendations

Time allocated to the BIIR collaboration has to be compensated by emergence of an adjunct PI who will handle the day-to-day life of the team.

- **Team name: Membrane dynamics and lymphocyte signaling**
- **Team leaders: M. Hai-Tao HE and M. Didier MARGUET**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	2	2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	4	4
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	4	4
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	2
N6: Number of Ph.D. students (Form 2.7 of the application file)	3	3
N7: Number of staff members with a HDR or a similar grade	2	2

- **Appreciation on the results**

This team is composed of two principal investigators, Dr. Hai-Tao HE and Dr. Didier MARGUET. This association represents a rare and optimal combination of state-of-the-art advanced microscopy together with a recognized expertise in the cell biology of the plasma membrane in living cells. The last ten years have seen the emergence of new concepts in the organization of the plasma membrane with a special focus on the existence of lateral lipid assemblies within biological membranes, a concept known as lipid rafts. The fine understanding of how these dynamic assemblies contribute to the various biological events that are initiated at the plasma membrane has since been one of the major challenges in cell biology. It is clear now that this challenge will only be resolved with the development of more sensitive and cell adapted techniques. The MARGUET/HE team has taken this path for the last few years by using and developing new biophotonic approaches to study the spatio-temporal complexity of the plasma membrane and its role in the signal transduction events occuring in immune cells and more particularly T lymphocytes. These aspects are particularly poorly studied in lymphocytes. As a result, the team has published several articles in high ranking journals in both disciplines and has gained national and international scientific recognition. Using spot-variation Fluorescence Correlation Spectroscopy (svFCS), the team could demonstrate the existence of a nanoscale lateral organization in the plasma membrane of living cells with the importance of two major lateral confining forces that are lipid-dependent nanodomains and the actin meshwork. They further showed that this nanoscale organization is essential to the activation of some signaling pathways such as the PI3 kinase-Akt signaling pathway in T lymphocytes in response to CD28 stimulation. With the same approach (svFCS), they also established the role of these nanodomains in the initiation of T cell antigen recognition process. In two collaboratives studies including one inside the CILM, they also showed the importance of the confinement of activated receptors in NK cells to allow self tolerance in innate immune lymphocytes. In a second set of collaborations, they published in several high impact journals the importance of the lipid-based partition of Fas and Fas ligand in Fas mediated death. The team has also an important activity in the development of new biophotonic instruments and analytical programs. In a close collaboration with scientists at the optic Institut Fresnel in Marseilles, they have developed methods aimed at better defining the cartography of membrane dynamics. To do so, they have implemented a new algorithm named MTT for “Multi Traget Tracing” to

track with high spatial resolution the motion of single fluorescent molecules. A project funded by a FP7-HEALTH European network (CARS Explorer project) aims at developing in the field of Raman spectroscopy an endoscope based on non linear optics and laser pulse phase shaping for functional in situ imaging. Finally, the team is involved in the QUITO project funded by a Ministery of Research Fund. It is based on quadric wave lateral shearing interferometry for quantitative phase microsocopy of living cells. Altogether the results obtained by the team during the last 4 years reflects its excellence in tackling fundamental cell biology questions with state-of-the-art biophysical technologies. It is remarkable that the team publishes high standing work both in biology and in biophysics.

The team co-authors 30 articles for the 2006-2011 period. It includes 5 reviews. 22 articles are signed in a dominant position by members of the team. The impact factor is very good with some articles in EMBO J, Nat Methods, EMBO Rep, J Cell Science, Blood…etc…Three publications have already been significantly cited.

Several papers are published in lower impact but nethertheless recognized journals in biophysics. Several books and methods chapters have been written. Four thesis have been delivered.

Several productive collaborations have been established with local groups at the CIML and with external scientists leading to several articles. There is a stable and longstanding collaboration with a team at the Institut Fresnel in Marseille, a key collaboration for developing new bi-photonic approaches.

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

The team leaders have been invited to many international meetings (6 per year on average). They also have been involved in the organization of several national meetings.

The team has recruited one permanent scientist in 2008 (CR1 INSERM). Four post docs (2 foreigners) and 3 Ph.D. students are members of the current team.

The team has been very well funded over the past four years with grants from the public and private sector at both national and European levels. Several post doctoral fellowships have been obtained (ARC, LNCC, EMBO).

Several other collaborations with foreign laboratories are also mentioned. D. MARGUET participates to a FP7 Integrated Program and the team to a FP7-HEALTH European network (CARS Explorer project).

Setting up the “Interactions Molecular en Milieu Vivant – IMV2” imaging platform which provides this technology to the local community at the CIML. The platform has been labeled by both the INCA and IBiSA.

- **Appreciation on the strategy, management and life of the team**

The team is part of the OPTITEC competitive research pole and develops industrial partnership (MKT and PHASICS) through the FP7-EU program and the Fond Unique Ministériel. Setting up the “Interactions Molecular en Milieu Vivant – IMV2” platform which provides this technology to the local community at the CIML.

- **Appreciation on the project**

The team will continue its exemplary transdisciplinary approach to tackle complex questions relevant to the organization of the plasma membrane in lymphocytes using state-of-the-art biophotonic technologies. They will keep focusing on the T cell signaling with the the study of in situ protein and lipids dynamics at the cell membrane. The team will devote its best effort on two specific aspects of T cell signaling. The first aspect will study the consequences of T cell receptor triggering upon engagement with pMHC. The second aspect consists in investigating the spatial orientation dynamics of the CD3 subunit cytoplasmic domains upon receptor engagement. These two aspects will be studied with a combination of cutting-edge technologies including FCS spectroscopy, polarized time-resolved fluorescence, holographic optical tweezers microsocope etc. Another set of studies will investigate how T cells convert analog input into digital molecular response upon activation. To do so, they will study the Ras signaling pathways to understand its spatial-temporal molecular organization. Again this will be done with the techniques mastered by the team from FCS derived techniques, single particle tracking, and multicolor 3D nanoscopy (dSTORM and PALM imaging). There is no doubt that this project is innovative and takes advantage of the state-of-the-art

technologies developed by the team over the recent years. Very few groups have investigated the role of membrane compartmentalization in signaling through these new biophotonic technologies. The possibility to follow these events at later times during endocytosis and the possible tracking of signaling events in moving endo-vesicles is quite an exciting and innovative prospect.

Several important grants have already been obtained for the years to come. The significant number of good publications in the last four years as shown by the number of citations and the impact factor of the journals in which they have been published should facilitate the allocation of new ressources.

The goals followed in the proposed project are quite innovative and should bring important new data on the role of lipid-based compartmentalization in T cell signaling. Mixing biophotonics with cell biology to study Ras signaling in living cells is a truly cutting edge project.

- **Conclusion**

  - Summary

This team represents one of the best exemples of how transdisciplinary approaches can be applied to the understanding of complex cell biology questions. This is demonstrated by the quality of the published work and the good level of funding. More collaborations should be developed locally to take advantage of this unique expertise at the CIML.

  - Strengths and opportunities

This team has a rare synergistic combination of cell biology and biophysical approaches. Very few teams have been able to organize such a synergistic combination of expertises. There is a strong demand for such approaches among cell biologists and clearly the role of the plasma membrane nanoscale lateral organization is key to the understanding of several major events in the cell biology of lymphocytes. The collaboration with the optic Fresnel Institute garanties the continuous development of cutting-edge technologies.

  - Weaknesses and threats

The inherent difficulties to study the lipids of the plasma membrane (lack of specific tools, need to overexpress probes, no direct visualization of the processes…).

The time demanding development of cutting-edge optical techniques. The high level of competition in the field.

  - Recommendations

Although the team has already published several articles with internal scientists at the CIML, it appears that more groups at the CIML could benefit from collaborating with the team. This team offers a rare local opportunity to better understand the role of nanoscale lipid-based membrane orgnaization in several processes studied by other CIML groups in immune cells. Therefore, these collaborations should be promoted and the recruitment of an additional staff engineer in physics, a demand from the team, should be strongly supported to develop the access to the imaging platform.

- **Team name: Inflammation biology group**
- **Team leader: M. Toby LAWRENCE**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	1	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	2	4
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	1
N7: Number of staff members with a HDR or a similar grade	1	1

- **Appreciation on the results**

The team leader joined the CIML in 2009 and thus, most of its activity was polarized on setting its lab. The committee believes it is premature to appreciate its recent work in terms of publication, thesis numbers and partnerships stability.

The team leader is developing a very ambitious and competitive program on NF-kB pathway in inflammation. However, unlike the vast majority of the groups involved in the field, he is focusing on signaling pathways leading to the resolution of the inflammation. This approach may facilitate his success.

As previously mentionned, the committee feels that it is premature to evaluate recent original publications that mostly originate from his previous position. However, based on the numbers of reviews (Curr Top Microbiol Immunol 2010, Cold Spring harbor perspect Biol 2009, Cytokine Growth Factor Rev 2009), it is obvious that Team leader is well recognized in the field of macrophage inflammation.

Team leader organized a very well structured team including a staff scientist, an assistant professor, a senior technician, all with tenure positions, four postdocs and 1 PhD student. Team leader wishes to increase the size of his team according to the strong and secure funding he recently collected. However, space allocated to his team (half module but requesting for a full module) may restrain his progression.

Again, probably because its integration at CIML is still recent, its interactions with other members of CIML are not obvious.

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

Team leader has already organized a very well structured team including a young staff scientist (CR1 CNRS), an assistant professor (MC UnivMed), a senior technician. In addition, postdoc fellowships (EU-Marie Curie, LNCC, FRM) indicates that Team leader attracted young scientist with local, national and international expertise.

Even though Team leader recently joined the CIML, he has been extremely successful in securing funding and aggregating young scientists in his team in a short period of time. The external funding support that he personnaly received is reaching more thant 2.5 million euros and includes very prestigious grant such ERC Young Investigator starting grant and two french ANR grants. He also collected grants to secure postdoctoral positions.

- **Appreciation on the strategy, management and life of the team**

The team is composed of about 10 persons. It was not clear how the three tenure scientists will organize the lab life and managed the postdoc programs.

One staff member is currently assistant professor at Université Méditerranée and will be able to link the group to university allowing additional PhD recruitment in the future.

- **Appreciation on the project**

The research program is extremely ambitious and has been favorably evaluated for funding by ANR and ERC. The program is devoted to the role of NF-kB pathway in inflammation and mostly focused on cancer. The project relies on the assumption that resolution of inflammation promotes protumoral activities such immunosuppression and tumor growth. Preliminary results indicate that NF-kB pathway activation is correlated to anti tumor immunity inhibition and reciprocally inhibition of the NF-kB pathway promotes anti tumor activities. The program will:

- Investigate the role of IKKb and p38 in tumor associated macrophages using two spontaneous cancer model ; pancreatic ductal adenocarcinoma and melanoma. The latter being developped by Dr Schmitt-Verhulst at CIML will clearly be a program that will bring the two teams to collaborate.

- Characterize molecular mechanism regulating TAM phenotypes using DNA microarrays, ChIP and ChIP-Seq. The need for bioinformatic tools dedicated to high-throuput genomics analysis may allow collaboration with the team of Pierre FERRIER at CIML.

Identification of genes in cancer cells linked to TAM phenotype using high-throughput RNAi screen.

- **Conclusion**

  — Summary

The committee was extremely enthusiastic on Team Leader research activities and projects. Even though the NF-¤B pathway is a highly competitive field; the committee felt that Team Leader was engaged in this very ambitious program with strong assets.

  — Strengths and opportunities

Not only Team Leader is seeking for in depth knowledge on the role of IKK in tumor-associated macrophages (TAM) using state of the art murine cancer models but he also developed unique high-throughput strategy for cancer cell genes linked with TAM. To carry out this vast program, Team Leader secured funding for the next 5 years including a prestigious ERC grant.

  — Weaknesses and threats

No particular weakness identified.

— Recommendations

The committee felt confident that CIML direction would quickly solve the issues of lab space, post-doctoral researcher recruitments as well as animal facility space in order to be in agreement with ERC grant policy and mostly not to jeopardize this ambitious program.

- **Team name: Genetic and structural analysis of T cell interactions**
- **Team leaders: M. BERNARD and Ms. Marie MALISSEN**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	4	5
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	4	4
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	2
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	3	3
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	2
N7: Number of staff members with a HDR or a similar grade	2	2

- **Appreciation on the results**

The lab is widely-regarded internationally, and has a sustained record of accomplishment that places it among the very best molecular immunology groups in Europe. Over the past review period, the lab continued to make original and high quality contributions, many in high impact journals such as Immunity and Nature Immunology. Main area of research were the structural mechanisms by the T cell receptor (TCR) can be cross-reactive; the profound dysregulation of T cell homeostasis and regulation caused by alterations in the T cell adaptor protein LAT; the refined definition of Dendritic Cell (DC) subsets; and the creation of the first strain of mice in which gamma delta T cell development could be visualized directly. In each of these areas, new and important discoveries were made. Among them, the wholly unexpected finding that post-thymic alterations in LAT function confer on T cells an antigen-independent responsiveness that provokes overt lympho-proliferative and inflammatory disease beautifully illustrates the capacity of high quality basic research to create new perspectives in clinical immunology. Likewise, the team's competence in mouse genetic manipulation has underpinned the capacity to provide major new insight into the complexity of DC subsets. Indeed, the team has provided the major effective foundation for mouse transgenesis and knockout technology at the CIML and their aspirations and ambitions in this area continue to grow with "next generation" insertional mutagenesis and ENU. In this regard, Dr Bernard MALISSEN has been a prime mover in the development of a new on-site animal facility that is due to open during the next review period.

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

The lab has a very high visibility. The team leaders jointly address major conferences to which they are invited, and both are in receipt of scientific honours, and of peer-reviewed external funding. The majority of this is awarded to Dr Bernard MALISSEN, and in part reflects the many national and international collaborations that follow from the excellence of the team's accomplishments. Dr Bernard MALISSEN is also a particularly influential participant in several boards. The lab has hosted 5 PhD students, 8 postdocs and 7 other researchers over the review period. The quantity of publication outputs reflects the activities of a very successful team; the impact of the outputs has been consistently high because of the creativity with which the team applies its high level of competence in basic research.

- **Appreciation on the strategy, management and life of the team**

The lab is characterized by very well considered strategy. Of note, the growth of research on LAT, on DC subsets, and on mouse genetics, coupled with changes in personnel has provoked the conscious decision to halt structural studies of TCR biology. This reflects reasoned leadership by the co-heads. The lab is extremely well funded, and benefits from the capable and substantial contributions of several senior scientists. Several trainees have progressed to run their own labs internationally. Additionally, the lab contributes greatly to the overall capabilities of CIML, particularly through the development of the mouse molecular genetics capabilities.

- **Appreciation on the project**

There is much discussion of a perceived need for biological research to translate into biomedical and clinical research. While success in such translation is to be welcomed, it has such an emphasis has the potential to limit the capacity of pure, curiosity-driven basic research to open up new perspectives relevant to human pathophysiology. This point is beautifully illustrated by this laboratory's program that, while focused fully on basic mouse immunology, has revised our perspective on how allergic immunopathologies may develop. Rather than reflecting defects in tolerance or deficiencies in regulatory T cells, certain "Autoimmune" diseases may instead result from a loss of intrinsic T cell regulation. Such work should continue, and the proposal to examine the underlying mechanisms of the LAT-associated lymphoproliferative disorder is enthusiastically welcomed. Likewise, the team proposes to use its state-of-the-art competences to further characterize mouse DC subsets, with the potential to understand mechanisms of tolerance and immunogenicity within tissues. This is important. No doubt there will be scope in both major project areas to uncover roles for uncharacterized modifier genes. This should be a particularly interesting area of the research program facilitated by the team's ongoing and effective investment in mouse mutagenesis and phenotyping. Overall, the proposed project is a world-leading investigation into basic immunology that is expected to generate very important and high quality results with both biological and clinical implications.

- **Conclusion**

— Summary

The lab heads are both highly accomplished scientists, with the track record of Drs Bernard and Marie Malissen being particularly outstanding. The lab productivity is excellent. The projects have a good gain/risk balance and are extremely likely to continue to lead to high profile discoveries.

— Strengths and opportunities

* Focus and shrewd strategic leadership of the laboratory.
* State-of-the-art expertise on the manipulation and analysis of mouse immune cells.
* A good mixture of hypothesis and discovery-based research faciliated by ENU technology.
* Uniqueness of mouse models, that provide new and unexpected clinical insights.

— Weaknesses and threats

The ENU approach is currently a great opportunity for the lab. It has required and will require a high investment, important resources and optimal screening strategies but is compensated by its upward potential. The decision on

whether to extend or reduce the commitment to this program will require the overall output to be evaluated in a few years.

- **Team name: Genomic instability and human hemopathies**
- **Team leader: M. Bertrand NADEL**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	3	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	2	2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	1
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	2
N7: Number of staff members with a HDR or a similar grade	1	1

- **Appreciation on the results**

The team leader is unanimously recognized as a world expert in follicular lymphoma.Indeed the lab has been instrumental in the understanding this desease, a work which has resulted in several landmark papers in journals such as J.Ex.Med,Leukemia and Plos Biology.They have shown that (14-18) translocations can be found in the blood of healthy individuals but also that these translocations are more frequent in farmers exposed to agricultural pesticides,such increase being due to abnormal clonal expansions of the (14-18) bearing B cells which may recapitulate at these early stages the first events leading to follicular development. Surprisingly they have recently shown that signal-joints which are by-products of V(D)J rearangements can re-integrate in the genome and create a putative oncogenic threat. Finally in collaboration with clinical departments they have identified a central role for c-Myc in T cell acute lymphoblastic leukemia thus providing a new therapeutic target for this devastating desease.

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

The team leader is highly active and has been invited in most international meetings on lymphomagenesis.The lab has hosted 3 post-doc and 3 PhD students over the review period. Collaborations with clinicians in Marseille and outside(Necker,La Pitié,St Louis,Bicetre) are central to the activity of the group allowing them to combine their precise molecular approach with an epidemiologic outlook.

- **Appreciation on the strategy, management and life of the team**

The head of the lab has a clear overview of what he wants to achieve.This is very important although the fact that they should concentrate on their field of excellence (follicular lymphoma) and not dilute too much their effort on other subjects such as T cell tumors has been discussed.The lab has been very successful in obtaining peer-reviewed grant support and has increased its size from 2006 to 2010 (5 to 11 persons) with the recruitment of one more senior scientist and one to come (CR1).

- **Appreciation on the project**

The team wishes to pursue his three topics of interest: on follicular lymphoma for which he has engineered a transgenic mouse model in order to mimick the sporadic (14-18) translocation events as they occur in humans.On T-ALL for which he wants to assess the role of c-Myc on the development and aggressivness of the desease. On the re-insertion of signal-joints in order to check whether these events can by their site of insertion next to oncogene be one of the causative event of leukemia and lymphoma.

- **Conclusion**

  - Summary

The head of the lab is an accomplished scientist. His work on follicular lymphoma has become a reference in the field. His expertise in molecular biology together with his epidemiological approach should allow him to unravel the precise steps leading to this desease.

  - Strengths and opportunities

State-of-the-art molecular and transgenic expertise with the access to clinical samples. Collaboration in France and whithin the CIML facility for wider approaches such as whole genome sequencing of FL and pre-FL samples.

  - Weaknesses and threats

The desire of the team leader to study T cell leukemia and the fact that while he has a world leading position in FL that he should maintain and reinforce he might have to face in this other field a very harsh competition.

- **Team name: Tissue inflammation and immunity**
- **Team leader: M. Philippe NAQUET**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	2	2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	2
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	1
N7: Number of staff members with a HDR or a similar grade	2	2

- **Appreciation on the results**

This team is focused on the analysis of the role of vanin molecules. Main discoveries during the past 5 years include:

∗ The demonstration through the analysis of vanin-1-deficient mice that vanin-1 is a major regulator of intestinal inflammation (J. Exp. Med., 2006). Vanin-1 also confers a significant protection against the development of colitis-associated colon cancer (Inflamm. Bowel Dis., 2010).

∗ The constitution of an important cohort of patients with Crohn's disease or ulcerative colitis. First results show that vanin-1 is highly overexpressed on colon mucosal tissues of ulcerative colitis patients.

∗ The demonstration that vanin-1 is cytoprotective for islet beta cells and regulates the development of type 1 diabetes (Diabetologia, 2008).

∗ The identification of a role for TGFb in the homeostasis of B cells and IgA production (J. Immunol., 2008).

From 2006 to 2010, team members have published 14 publications in peer-review Journals, among which 6 as first and/or last author. Most significant papers were published in J. Exp. Med. (2006), J. Immunol. (2008), Eur. J. Immunol. (2007, 2008) and Diabetologia (2008). Team members have developed numerous collaborations outside as well as inside CIML.

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

The PI has recently co-organized an EMBO meeting on the theme: "immunity and metabolism" (January 2011). The PI is director of the doctoral school in life and health sciences since 2008 and is in charge of the immunology master program since 2004. During the past 5 years, 2 PhD have achieved their thesis and 2 are currently working in the laboratory. The team members have been able to raise significant funding since 2006. Funding sources include 3 grants from INCa (2 with a team member as coordinator), 1 grant from the ARC, 1 AFA contract as coordinator, 1 grant from the European Community as participant. Team members have developed long term collaborations with international (USA, Portugal, Italy, Holland), national (Paris, Lille, Nice) and local teams.

- **Appreciation on the strategy, management and life of the team**

The team includes 2 researchers and 1 technician with a permanent position. A researcher (CR1, CNRS) is currently on sabbatical leave. An assistant engineer has been hired on March 2011 funded by the SANOFI-AVENTIS / CIML network.

- **Appreciation on the project**

During the next 5 years, team members are planning to decipher vanin function in the context of inflammatory and immune-mediated diseases. They plan to (1) Analyze vanin-mediated modulation of inflammation pathways, notably the relationship between vanin and regulation of PPARg expression and/or activity, (2) Evaluate the involvement of vanin-1 in human inflammatory bowel diseases, (3) Develop novel tools including vanin-3-deficient mice to explore the function of vanin-3 in hematopoietic cells with a specific emphasis on myeloid cells, (4) Explore the contribution of vanin molecules to the metabolism of lipids.

All these projects are in line with their previous projects. They will need to rapidly develop the animal models required to achieve their goals. They have already set-up collaborations with numerous teams outside and inside the CIML that will help them reaching their goals.

- **Conclusion**

— Strengths and opportunities

* Development of animal models (KI/KO, ENU) that will enable them to achieve their goals.
* Strong links between fundamental and clinical research.
* A few good publications during the past 5 years (J. Exp. Med., JI, EJI).
* Ability to develop fruitful and pertinent collaborations outside the CIML.
* Opportunity : controlling inflammation is a major issue in public health.

— Weaknesses and threats

* The team does not include a full-time researcher, i.e. without teaching duties.
* Too many projects for a relatively small team.
* The project on the role of vanin in the metabolism of lipids ?

— Recommendations

* Keep focusing on a limited number of projects.
* Strenghten collaborations within the CIML.

- **Team name: Membrane dynamics and lymphocyte signaling**
- **Team leader: M. Philippe PIERRE**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	4	4
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	3	3
N7: Number of staff members with a HDR or a similar grade	1	1

- **Appreciation on the results**

The team is currently composed two senior researchers, three PhD students and four postdocs. The laboratory concentrates on the cell biology of dendritic cells with specific focus on molecular mechanisms of maturation and antigen presentation. Specifically this involves aspects of translational control, MHC trafficking and detection of microbial signals. The work can be described as state of the art cell biology in the context of immunology.

In one key study the group described DALIS, which are aggresome-like maturation-induced structures that harbour misfolded proteins and presumably act as a store for antigens to be presented. The papers in this field were true landmarks and the three Lelouard et al. papers in Nature and JCB received enormous attention are widely cited and were commented on in Nature. These are landmark studies that virtually opened new avenues of cell biology / immunology. Regarding transcriptional regulation the team was one of the first to investigate the maturation-induced micro RNA 155 and in a PNAS paper they identified IL1 as a functional target. This was an important and widely recognized finding in a very competitive field. It is important to note that many of the molecular findings arose from unbiased screens, demonstrating the ambition and the capability of the group to work with a true systems biology attitude. This does not only include standard technology but also the development of novel and original technology. The most prominent example has been published in Nat Methods where the group described a new approach to monitor protein synthesis (SUnSET) that is already widely used and received attention from researchers in many fields. These achievements are remarkable. There is a breadth and spectrum of methodology and scientific interests that is rarely found and the work covers state of the art molecular studies as well as the organismic implications.

Altogether it is beyond doubt that the team works at the cutting edge in the field of cell biology / immunology. It is one of the few places where cell biology is performed at the highest technical level by almost purely focusing on physiologically relevant primary cells and in certain cases in vivo models.

Between 2006 and 2011 the laboratory published 17 research articles and 1 review. 9 of the papers had Pierre or Gatti listed as senior author. The journals are excellent throughout, including Nat Methods, J Cell Biol, EMBO J, PNAS, MCB

etc.. This is a high level productivity for the group size and most importantly, most of the papers are heavily cited and commented on as reflected by editorials and 3 commented papers by F1000. It is especially noteworthy that Evelina Gatti is listed as senior author in some cases indicating that work done by "staff scientists" is adequately appreciated in the group.

There are stable and productive partnerships within CIML as exemplified by a co-senior authored paper with the Gorvel's group. The team leader has a widely appreciated reputation as an open and interactive researcher.

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

The team is international (Germany, France, Italy, Japan, Portugal) indicating that the team is internationally known and renowned. Collaborations are local but also international, with partners in various fields also outside immunology.

The team leader is invited to most relevant meetings in the field. This includes prestigious events like Gordon conferences, EMBO workshops and the international dendritic cell conference. This is the most convincing demonstration of international reputations (even in the absence of awards).

The team is highly international. Eight nations during the review period. This is beyond doubt highest standard.

The team is enormously well funded by national and international sources. This includes very competetive grants like a HFSP program grant and the EMBO Young Investigator award. 25 grants in the review period!

The HFSP project and two EU (FP6 and FP7) grants demonstrate european and global integration.

Two patents related to the SUnSET method are held by the PI, with a considerable likelihood that these develop into commercially relevant products.

- **Appreciation on the strategy, management and life of the team**

Papers that are last authored by the "staff scientists" are very good indications of a positive group management, considering the career development of the group members. Also co-author papers are always authored by at least two members of the team, indicating that the work of the team members is adequately appreciated.

See above – the PI is well known as open minded communicative and participation in the organization of several workshops and conferences demonstrates a good standing in the scientific community.

The team is involved in the FP7 network aiming at the identification of novel biomarkers. See also above regarding the patents of the SUnSET system.

No information is available here. Three PhD students are trained in the group.

- **Appreciation on the project**

There is no doubt that the laboratory will continue to make important contributions on the field of molecular mechanisms of antigen presentation by dendritic cells. A focus will be the regulation of stress pathways using stressor reporter mice and investigating the role of GADD34 which direcrly influences the translational machinery. This will be done using a mixture of mouse genetics and in vitro cell biology and findings will be challenged in collaboration with the Gorvel and the Lecuit labs in the context of infections. The laboratory will also continue working on its previous key finding that DALIS act as antigen storage compartments in dendritic cells and investigate the microbisl induction of DALIS as well as the pathway how they are related to actual antigen processing and presentation. Evelina Gatti will continue to investigate MARCH ubiquitin ligases and extend the studies beyond the now well established funtion of MARCHI to other family members especially MARCH IX. A key to deciphering the function of MARCH will be to identify new molecular targets. Altogether this is a rich and creative work program, the technical expertise is given and it is unlikely that the lab will not continue to increase productivity.

Considering the track record of funding that the group has and the increasing rate of publication output it is certainly very likely that resources will not be an issue in the Pierre group.

The goals in the research program are cutting edge and in the field of cell biology of antigen presentation the Pierre group is at the very forefront. The group will translate its previous findings into a more physiological context by using infectio models and also by focussing on different dendritic cell subtypes.

- **Conclusion**

  - Summary

The team is a role model for modern immunology. It works at the interface to cell biology and technically implements biochemical approaches, imaging studies, functional screens and molecular biology. The work is internationally well recognized and will certainly continue to be so.

  - Strengths and opportunities

The projects offer the chance to obtain a holistic view of a number of novel cell biological findings in the context of antigen presentation.

  - Weaknesses and threats

Although the three projects of the team display a good synergy so far, it will be a challenge to remain coherent as a group when the projects move into more detailed molecular analysis.

  - Recommendations

The imaging branch could be further developed and it might be useful to extend the system biology approach towards proteomic studies. This could be especially helpful to analyse the function of DALIS (provided that it is possible to isolate these organelles). Overall it is difficult to see room for improvement as the team is well integrated into the institute, scientifically original and successful and apparently supporting the career development of its members.

- **Team name: Human B cell differentiation: physiological and pathological aspects**
- **Team leader: Ms. Claudine SCHIFF**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	2	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	2
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	1
N7: Number of staff members with a HDR or a similar grade	1	1

- **Appreciation on the results**

The team was a medium sized team that recently downscaled significantly due to the approaching retirement of the PI. The group now consists of three staff scientists, one PhD student and one postdoc. The laboratory is investigating molecular and cellular players that act in the stem cell niche to guide and maintain B cell differentiation and selection. The particular focus of the lab is elucidating the function of the pre B cell receptor. The lab showed that the pre B cell forms a “synapse” with bone marrow stroma cells that is essential for information transfer between the cells. The synapse harbors components that are partly analogous to the immunological synapse and it includes the pre B cell receptor as well as integrins. In the recent years the Schiff laboratory made one decisive contribution to the field and identified the ligand of the pre B cell receptor on the bone marrow stroma cells to be galectin1, a member of the S-lectin family. This finding was a landmark as numerous labs were looking for this ligand and some even douted its existence. Although there were many labs that proposed ligands the Schiff lab was the only one to thorouhghly follow their finding and in a Blood paper (2009) the team published also the pohenotyope of the respective knockout mouse and found a defect in the expected B cell development pathway. This finding is really essential and it is somewhat surprising that it was not publsihed in an even more prominent journal, but this can possibly be attributed to the huge controversies and competitions in the field. Nevertheless, it is remarkable how thoroughly and persistent the Schiff lab followed and is planning to continue to follow this finding. NMR structures of the interaction were prepared and the involvement of the integrins as glycosylated binding partners was investigated in detail. The lab has also an interest in the possible involvement of the bone marrow niche in pathological processes like malignant transformation and is further trying to use the newly developed tools to map the chreography of cellular interactions during B cell development in the bone marrow. Together, the Schiff laboratory is well focused and has a very sharp profile. The data cannot be ignored in the field and it is a very wise idea to focus the efforts during the final period of the lab and solidify the data so that others can develop the concept further.

The laboratory co-authored 11 research articles during the review period, 3 were last authored by the PI. One review was published, as well as one book chapter and 1 patent has been filed. The output is not enormous but from the report it becomes obvious that many data are to be published soon.

There are well established collaborations within the CIML. One publication in J Exp Med was a joint project with the Nadel'team on lymphomagenesis. Outside the institute the laboratory is well connected on the national and international level.

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

The team leaders are regularly invited to top conferences, including keystone meetings. This demonstrates the strong standing of the laboratory in the field and underlines the importance of the recent findings.

The team has newly recruited one permanent scientist, apart from that it has mainly downscaled, which is adequate in the light of the approaching retirement of the PI.

The team was well funded but slowed down this activity.

There are numerous long standing collaborations with international partners but no new common grant initiatives. Likely this reflects that the gradually projects are handed over to partners, which is very reasonable.

One patent has been filed – to use galectin1 as a biomarker for chondrosarcoma and osteosarcoma.

- **Appreciation on the strategy, management and life of the team**

It appears that there is very good mentoring of students and postdocs that obviously all found good positions.

The team is part of the histology platform and the collaborations with clinicians where the BLNK and XIAP mutations have been identified are appreciated.

Participation in the histology platform is essential especially considering the expertise of the laboratory in the non-trivial histological processing of bone marrow samples and the development of new biomarkers.

- **Appreciation on the project**

The plan to focus the team activity on "wrapping up" the characterization of the Galectin-Pre B cell receptor interactions, continue the characterization of the bone marrow stroma microenvironemnt and completing the initiated development of mouse tools is very reasonable. Also the attitude to manage the many collaborations in a manner to potentially "hand over" projects to partners makes true sense.

The proposed goals are very reasonable and the management of the collaborations alone will be quite a logistic challenge. Regarding the originality of the findings the scientific value cannot be over-estimated. The finding of the Pre B cell receptor ligand is an absolute key and important for the field. Deciphering the physiological importance of this interaction, investigating the cellular context in situ and possibly finding implications for pathology are highly important.

- **Conclusion**

  - Summary

The stategy of the team is a very good example and a role model how to responsibly scale down and focus a laboratory when the PI is about to retire. The findings of the last years are absolutely significant and many things are about to be published at the end of the period.

— Strengths and opportunities

A very broad approach – from the structural level of one molecular interaction to the cellular context in situ, to the importance on the organismic level to the involvement in pathological conditions. High quality work with very state of the art and solid approaches throughout.

— Weaknesses and threats

The challenge will be to hand over the projects so that the work finds its proper continuation.

— Recommendations

It will be essential to start outsorcing projects in a responsible manner and develop an adequate career plan for the postdocs and the staff scientists.

- **Team name: Molecular bases for T lymphocyte function**
- **Team leader: Ms. Anne-Marie SCHMITT-VERHULST**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	5	5
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	2	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	2	2
N6: Number of Ph.D. students (Form 2.7 of the application file)	4	3
N7: Number of staff members with a HDR or a similar grade	4	4

- **Appreciation on the results**

This team is working on the molecular mechanisms allowing the differentiation of naïve CD8+ T cells into efficient effectors. Main discoveries during the past 5 years include:

∗ The analysis of the role of peptides in the TCR recognition of MHC class I alloantigens (EJI, 2006 ; Embo J., 2007).

∗ The demonstration that both the intensity of TCR stimulation and signals received from the IL-2 receptor contribute to the generation of cytotoxic CD8+ effectors (EJI, 2006; JI, 2006).

∗ The development of an elegant mouse model of inducible melanoma (Cancer Research, 2006).

∗ The demonstration that CD8+ T cells and NK cells cooperate to control tumor growth (JI, 2007; Immunology, 2010).

* The analysis of the factors (intrinsic versus adaptive immunity-related) controlling tumor aggressiveness in their mouse model of inducible melanoma (Cancer Res., 2010).

From 2006 to 2010, team members have published 13 publications in peer-review Journals, among which 9 as first and/or last author. Most significant papers were published in Cancer Research (2010), J. Immunol. (2006), Eur. J. Immunol. (2006, 2007). Team members have developed excellent collaborations outside as well as inside CIML.

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

Team members have been invited or have participated to numerous national and international meetings. During the past 5 years, 2 PhD have achieved their thesis and 3 are currently working in the laboratory. The team members have been able to rise significant funding since 2006. Funding sources include 5 grants from INCa (2 with the team leader as coordinator), 1 grant from the ARC, 1 ANR contract as coordinator, 2 grants from the European Community as

participant Team members have developed long term collaborations with international (Belgium), national (Paris) and local teams.

- **Appreciation on the strategy, management and life of the team**

The team includes 4 researchers and 1 technician with a permanent position. A post-doc from the lab who has obtained an important grant from the ANR is currently applying for a permanent position. The team will remain in its present structure up to the end of 2012. The team will be closed during the year 2013 upon retirement of the principal investigator.

- **Appreciation on the project**

During the next 2 years, team members are planning to evaluate CD8 T lymphocyte differentiation and function in face of tumor development. They plan to:

* Decipher the epigentic events leading to the differentiation of naive CD8 T cells into effector and memory lymphocytes.

* Study the influence of the tumor microenvironment in the behavior of infiltrating lymphocytes. They have developed tools that will allow them to visualize the differentiation of CD8 T cells in vivo.

* Evaluate the basis for CD8 T cell migration within tumors.

All these projects are well in line with their previous projects. They have developed the animal models to achieve their goals. The have developed collaborations with several teams inside the CIML that will help them reaching their goals.

- **Conclusion**

  - Strengths and opportunities

* Development of a pertinent and powerful mouse model of inducible melanoma.

* Development of numerous other animal models that will enable them to achieve their goals.

* A few excellent publications during the past 5 years (Cancer Research, JI, EJI).

* Ability to develop fruitful and pertinent collaborations outside as well as inside CIML.

* Recruitment of a post-doc that has recently obtained an important grant from the ANR.

  - Weaknesses and threats

* The team will be closed during the year 2013 : only 2 years left and still a lot of different projects.

– Recommendations

∗ The mouse model of inducible melanoma they have set-up is pertinent and powerful. The team should keep focusing on a limited number of projects aimed at deciphering the immune response in this model.

- **Team name: From stem cells to macrophages**
- **Team leader: M. Michael SIEWEKE**
- **Staff members**

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

- **Appreciation on the results**

This is a well-established team and well renowned at the national and international levels in the competitive field of stem cells and commitment. Over the past 4 years, the team has focused its research activities on the study of cell proliferation and differenciation ; mainly, regarding the regeneration of the hematopoietic stem cells (HSC) and their myeloid differenciation. The major findings were : 1)-That cytokines are able to instruct cell fate rather than just having permissive activity : the transcription factor (TF) MafB acts as a sensitivity threshold for the cytokine M-CSF , where down-regulation of MafB enables this cytokine to instruct myeloid fate in HSC. (Cell, 2009) ; 2)-That MafB driven macrophage differenciation is controlled by SUMO-modification and involved antagonism with the factor c-Myb and inhibition of cell cycle progression (Mol Cell Biol, 2006, 2007) ; 3)-That combined deficiency of the 2 TF, MafB and c-Maf, leads to extended proliferation and expansion of mature monocytes and macrophages in culture, over a period of 1 year ! Upon transplantation they were non-tumorigenic and contributed to functional macrophage populations in vivo (Science, 2009). These expanded mature cells may provide an attractive alternative to differentiated stem cells in cell therapy (Patented)

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

This team is well renowned worldwide for its work and exceptional contributions to the field of stemm cells and commitment. Numerous high impact papers have been published during these last years (9), as in MCB, PNAS, Embo, Gene and Dev, Cell and Science. The team leader has been invited speaker at various national and international meetings, important funding have been raised (Equipe FRM, ANR, Inserm Transfert). In addition, the team leader owns

2 patents. The team has trained numerous students: 5 DEA, 6PhD and 4 Postdocs fellows. The team leader is a very enthousiastic person and this is shared by his team. Overall, this research group has achieved a terrific work.

- **Appreciation on the project**

For the coming years, the group aims at focusing on investigating lineage commitment of HSC, self-renewal and reprogramming in mature macrophages and the role of monocyte-macrophage subtypes in inflammation and tissue regeneration. They have developped several novel protocols to analyze transplanted purified HSC, in vivo and in vitro. The « hematopoietic niche » will then be studied, thanks to the CIML video-microscopy platform. The committe felt that the homeostatic in vivo control of macrophages double-deficient for both TF (MafB and c-Maf) should be investigated.

Also, they will investigate the reprogramming of these populations into closely or related cell types by over-expressing an appropriate cocktail of TF. The committee recognizes that this represent a scientific challenge, however, the team is well equipped in terms of critical mass and up to date methodologies to face such a challenge at the best level and in the context of the international competition.

A novel area of research was also proposed, the generation of beta cells.

- **Conclusion and recommendations**

The committee was unanimously impressed by the overall work of this team and the scientific progress obtained.

- **Team name: Natural Killer cells and Innate Immunity**
- **Team leader: M. Eric VIVIER**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	2	2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	4	4
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	4	4
N6: Number of Ph.D. students (Form 2.7 of the application file)	3	3
N7: Number of staff members with a HDR or a similar grade	3	3

- **Appreciation on the results**

The lab head is one of the most prominent international experts in the field in NK cell biology. The contributions from his laboratory are exceptional. Most recent achievements include evidence for an education process in human NK cells, the identification of NKp46 has an marker for mouse and human NK cells and the generation of mouse lines allowing specific ablation of this subset, the discovery of a new subset of innate lymphoid cells in the gut, and the demonstration of the role of S1P5 in NK cell trafficking. The lab is also contributing to innovative therapy using anti-KIR mAb treatment, and the links with local clinical teams in Marseille seem serious, valid, and effective, providing a role model for more extensive such interactions by other laboratories at the CIML. As one metric of the lab's accomplishments, there is a strong publication record in high-impact journals (Immunity, PNAS (x2), Nat. Immunol. (x2), J. Exp. Med). Overall, the impact of the lab on the field is profound, internationally recognized, and likely to prove long lasting.

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

The lab has an excellent visibility. The team leader is a recipient of several prestigious awards and has participated in many international meetings (>20 in the past 3 years). The lab has hosted 7 PhD students and 7 postdocs over the review period. The lab is extremely well funded, and the team leader is a recipient of an advanced grant from the European Research Council. The team leader, who is also the head of the CIML, has been capably assisted in the development of his research program by several senior scientists. In this regard, there is a proposal that the management of the team be substantially assisted by S. Ugolini. Ms. Ugolini has published actively with the team leader over the past several years, including senior authorship on high impact research papers in PNAS and Science Signaling and on reviews in influential journals such as Nature and Immunological Reviews. Her focus is on the biophysical and biochemical aspects of NK cell regulation, and these skills complement those of the team leader. She

is described as being a principal investigator on external grant funding to support such work, and has evidently participated substantially in student supervision. Hence, the proposal would seem prima facie to be appropriate.

- **Appreciation on the project**

It is by now acknowledged that NK cells are extremely important, with roles extending well beyond the rapid cytolysis of tumor targets to integrated roles in myriad immune responses. Moreover, NK cells have proved a major foundation for the discovery of new innate lymphocyte subsets. Therefore, there is much to do. In choosing research questions, the laboratory has a record of taking on ambitious yet incisive studies and this trajectory continues in the current proposal. The scientific project is ambitious, well articulated and relies on the competence and confidence to apply state-of-the-art approaches. Critical questions related to NK cell development and function will be addressed. The lab has heavily invested in the ENU mutagenesis technology. This approach has led to the generation of two interesting mouse models for the study of NK cell tolerance. The project will also benefit from local expertise in fluorescence correlation spectroscopy and other imaging modalities. The NKp46-DTR-EGFP mouse strain that the lab has generated will offer the opportunity to study the role of NK cells in various contexts. The team will also elaborate of the previous characterization of an NKp30 ligand and seek to identify other NCR ligands. Overall, the proposed project is expected to generate very important and high quality results on multiple aspects of NK cell biology.

- **Conclusion**

  - Summary

The lab head is a highly accomplished basic scientist, with an outstanding track record. The lab productivity is excellent. The projects have a good gain/risk balance and are extremely likely to continue to lead to high profile discoveries. There seems a genuine commitment to meaningful clinical collaborations that may provide a practical foundation for increased translational scope of science at CIML.

  - Strengths and opportunities

Expertise on both human and mouse NK cell biology. A mixture of hypothesis and discovery-based research with ENU technology. Uniqueness of mouse models. Commitment to test innovative therapy based on KIR blockade, and a commitment to develop substantive clinical research collaborations.

  - Weaknesses and threats

The ENU approach is currently a great opportunity for the lab. It requires a high investment, important resources and optimal screening strategies but is compensated by its upward potential. The decision on whether to extend or reduce such program will require the overall output to be evaluated in a few years.

Intitulé UR / équipe	C1	C2	C3	C4	Note globale
CIML - CENTRE D'IMMUNOLOGIE DE MARSEILLE - LUMINY	**A+**	**A+**	**A**	**A+**	**A+**
TOLL-LIKE RECEPTORS IN IMMUNITY [VIVIER-ALEXOPOULO]	A	A	Non noté	B	B
FROM LYMPHOID ORGAN STRUCTURE TO LYMPHOCYTE MIGRATION [VIVIER-BAJENOFF]	Non noté	A	Non noté	A+	A+
DENDRITIC CELLS AND ANTIVIRAL DEFENSE [VIVIER-DALOD]	Non noté	A+	Non noté	A+	A+
INNATE IMMUNITY IN C. ELEGANS [VIVIER-EWBANK]	A+	A+	Non noté	A+	A+
LYMPHOCYTE DIFFERENTIATION AND THE CONTROL OF GENE EXPRESSION & RECOMBINATION [VIVIER-FERRIER]	A	A+	Non noté	A	A
MOLECULAR BASES OF AUTOPHAGIC CELL DEATH [VIVIER-GOLDSTEIN]	A	A+	Non noté	A	A
IMMUNOLOGY AND CELL BIOLOGY OF BACTERIA-HOST INTERACTIONS [VIVIER-GORVEL]	A+	A+	Non noté	A+	A+
MEMBRANE DYNAMICS AND LYMPHOCYTE SIGNALING [VIVIER-HE-MARGUET]	A	A	Non noté	A+	A+
INFLAMMATION BIOLOGY GROUP [VIVIER-LAWRENCE]	Non noté	A+	Non noté	A+	A+
GENETIC DISSECTION OF THE FUNCTION OF T CELLS AND DENDRITIC CELLS [VIVIER-MALISSEN]	A+	A+	Non noté	A+	A+
GENOMIC INSTABILITY AND HUMAN HEMOPATHIES [VIVIER-NADEL]	A+	A+	Non noté	A+	A+
TISSUE INFLAMMATION AND IMMUNITY [VIVIER-NAQUET]	A	A	Non noté	A	A
DENDRITIC CELL BIOLOGY [VIVIER-PIERRE]	A+	A+	Non noté	A+	A+
B CELL DIFFERENTIATION: PHYSIOLOGICAL AND PATHOLOGICAL ASPECTS [VIVIER-SCHIFF]	A	A+	Non noté	A	A
MOLECULAR BASES FOR T LYMPHOCYTE FUNCTION AND ANTI-TUMOR RESPONSES [VIVIER-SCHMITT-VERHULST]	A	A	Non noté	A	A
MACROPHAGE AND STEM CELL BIOLOGY [VIVIER-SIEWEKE]	A+	A+	Non noté	A+	A+
NK CELLS AND INNATE IMMUNITY [VIVIER-VIVIER]	A+	A+	Non noté	A+	A+

C1 Qualité scientifique et production
C2 Rayonnement et attractivité, intégration dans l'environnement
C3 Gouvernance et vie du laboratoire
C4 Stratégie et projet scientifique

Statistiques de notes globales par domaines scientifiques

(État au 06/05/2011)

Sciences du Vivant et Environnement

Note globale	SVE1_LS1_LS2	SVE1_LS3	SVE1_LS4	SVE1_LS5	SVE1_LS6	SVE1_LS7	SVE2 _LS3 *	SVE2_LS8 *	SVE2_LS9 *	Total
A+	7	3	1	4	7	6		2		30
A	27	1	13	20	21	26	2	12	23	145
B	6	1	6	2	8	23	3	3	6	58
C	1					4				5
Non noté	1									1
Total	**42**	**5**	**20**	**26**	**36**	**59**	**5**	**17**	**29**	**239**
A+	16,7%	60,0%	5,0%	15,4%	19,4%	10,2%		11,8%		12,6%
A	64,3%	20,0%	65,0%	76,9%	58,3%	44,1%	40,0%	70,6%	79,3%	60,7%
B	14,3%	20,0%	30,0%	7,7%	22,2%	39,0%	60,0%	17,6%	20,7%	24,3%
C	2,4%					6,8%				2,1%
Non noté	2,4%									0,4%
Total	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%

*** les résultats SVE2 ne sont pas définitifs au 06/05/2011.**

Intitulés des domaines scientifiques

Sciences du Vivant et Environnement

- **SVE1 Biologie, santé**
  - **SVE1_LS1 Biologie moléculaire, Biologie structurale, Biochimie**
  - **SVE1_LS2 Génétique, Génomique, Bioinformatique, Biologie des systèmes**
  - **SVE1_LS3 Biologie cellulaire, Biologie du développement animal**
  - **SVE1_LS4 Physiologie, Physiopathologie, Endocrinologie**
  - **SVE1_LS5 Neurosciences**
  - **SVE1_LS6 Immunologie, Infectiologie**
  - **SVE1_LS7 Recherche clinique, Santé publique**
- **SVE2 Ecologie, environnement**
  - **SVE2_LS8 Evolution, Ecologie, Biologie de l'environnement**
  - **SVE2_LS9 Sciences et technologies du vivant, Biotechnologie**
  - **SVE2_LS3 Biologie cellulaire, Biologie du développement végétal**

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Marseille, le 26 Avril 2011.

Observations de portée générale sur le rapport d'évaluation (General comments on evaluation).

We thank the AERES committee for the very positive comments on the research conducted at CIML and on the management of the Center.

There are few points that we would like to address as follows.

OVERALL APPRECIATION OF THE RESEARCH UNIT

1. Weaknesses and threats : The only general weakness that came out from our discussion with researchers, students and technical staff of the CIML was a request for more dialogue with the direction. The committee feels that -given the size of the center- the director should be surrounded by 4-5 group leaders who can meet regularly in order to tackle the different problems when they come out. Indeed, flexibility is key for such a big structure full of talented people to work efficiently.

These points are well-taken.
Regarding the dialogue at CIML, a meeting with the Director and the "College de Direction" is organized on a monthly basis. All categories of staff members (students and post-docs, research assistants, researchers) are represented by one or more colleagues. Thanks to this organization, there have been many examples of discussions leading to common decision.
Regarding the proposal from the committe, we would like to re-emphasize that the CIML director is indeed "surrounded" by all group leaders during monthly meetings. At this occasion, CIML group leaders are asked to provide their feedbacks on CIML management and strategy. As a consequence, the decisions taken at CIML most often reflect a consensus. In the case of divergence, the decision is ultimately taken by the Director as a part of his mission of management of the Center.

2. *Recommendations to the head of the research unit*

* *To give -if possible- to the laboratories that have built a scientific platform the technical support they need so that they can properly transfer their knowhow to their colleagues without seeing their own research affected.*

This point might concern a single team at CIML; it has been discussed at several occasions directly with the group leader.

* *To elaborate precise rules for the replacement of available space after the departure of team taking into account the promotion of inside researchers as group leaders.*

When space is available at CIML, international open calls are launched and rules are well-established.

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* *To accompany the closing of Ms. Schmitt-Verhulst's team that has very exciting results on the molecular bases for T lymphocyte function in melanoma by helping her to transfer her animal models and the scientists associated to her team to other(s) groups in the center. Indeed, we felt that it would be deleterious for the CIML to loose this research line.*

* *On the same line, to make sure that the research on B lymphocytes is not lost once Ms. Claudine Schiff retires. We thus strongly recommend to the CIML director to actively search for a group leader working in the B cell field.*

We will take these recommendations into consideration when the call for new CIML group leaders is launched.

* *To provide the proper help to Ms. Lena Alexopoulo for her to reinforce her team that has suffered a dramatic reduction in size. We also recommend to the CIML director to encourage her to focus her research on the projects for which she can be at the forefron*t.

This point will be discussed in detail with L. Alexopoulou as soon as possible.

* *To continue keeping the group leaders happy.*
* *To reinforce the PhD program that was recently created.*

Thank you for these positive comments.

SPECIFIC APPRECIATION ON THE RESEARCH UNIT

- Pierre Ferrier team.

Page 20:
Regarding the following statement: *"The team leader lists an aspiration to improve the impact of the publication record, and this is likely to be threatened without some improved focusing of the research goals"* (lanes 3-5), it has to be noted, however, that this lab just had (ie, shortly after the AERES visit) a research article accepted for publication in Nature Structural & Molecular Biology, a leading journal in the fields of genomics and molecular biology.
The three following sentences on lanes 6-9 are irrelevant to this team, and should be removed: "*The ENU approach is currently a great opportunity for the lab. It requires a high investment, important resources and optimal screening strategies but is compensated by its upward potential. The decision on whether to extend or reduce such program will require the overall output to be evaluated in a few years."*

- Lena Alexopoulou team.

On page 7, table with staff members, regarding the past members of this team the correct numbers are as follows:
N3 postdocs: 5 (and not 0 as it is written)
N6 PhD students: 2 (and not 1 as it is written)

- He & Marguet team

We are delighted with the appreciation and encouragements we have received from the AERES committee.
We would like to request a slight modification of the following statement, page 26, 2nd paragraph, *"...The impact factor is very good with some articles in EMBO J, Nat Methods, EMBO Rep, J Cell Science, Blood...etc...Three publications have already been significantly cited"*. The paper we published in Nat Chem Biol (Lasserre et al 2008) is missing in the list. We wish this paper to be included because it very significantly reflects the scientific interests of the group and is also among those of our publications that received a significant number of citations".

- JP Gorvel team

In response to a specific recommendation from AERES committee, an important decision was taken during the past four weeks. In Dallas, a new director has been appointed, Yon-Jun Liu, from Houston. His strategic research program is different from that of the former director Jacques Banchereau. YJ Liu pushes forward cancer and HIV vaccines. This does not fit any

longer with my "mise à disposition" contract at Baylor, which is dedicated to bacterial infectious diseases and cell biology of vaccines. In Marseille, the IHU (Institut Hospitalo-Universitaire) in tropical Infectious diseases has been created in April, which opens up several possibilities to develop translational research in the frame of the IHU to continue our scientific program aiming at bridging Microbiology and human Immunology as planned in the project section of the EARES document. Although we are going to continue to collaborate with the Baylor at Dallas on some aspects of the Cell biology of vaccines (HIV), my decision in agreement with the Baylor has been to cancel my move to Dallas and to focus on translational research at the IHU in Marseille. Therefore, I will keep my group leader position at CIML full time.

- G. Chimini team

We would like to modify the sentence *"As the office is just established results are only expected during the next review period"* with the following "Though the office is of recent institution it has already proven efficient by the establishment of an institutional partnership with industry that includes several teams at the CIML".

At the strength and opportunity paragraph (page 13 middle), we would like to introduce the following sentence : "The establishment of institutional partnerships that integrate several CIML teams is a distinctive achievement since it intensifies in-house collaboration on ambitious and collective scientific goals."

Pr. Eric VIVIER
Director of CIML

p/o

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