Immunité et cancer

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on unit:

Cancer Immunity

Under the supervision of the following institutions and research bodies:

Institut Curie

Institut National de la Santé et de la Recherche Médicale

January 2013

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

Research Units Department

President of AERES

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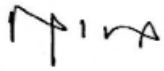


Pierre Glaudes

The president of AERES "signs[...], the evaluation reports, [...]countersigned for each evaluation department by the relevant head of department (Article 9, paragraph 3, of french decree n°2006-1334 dated 3 november 2006, revised).

Grading

Once the visits for the 2012-2013 evaluation campaign had been completed, the chairpersons of the expert committees, who met per disciplinary group, proceeded to attribute a score to the research units in their group (and, when necessary, for these units' in-house teams).
This score (A+, A, B, C) concerned each of the six criteria defined by the AERES.
NN (not-scored) attached to a criteria indicate that this one was not applicable to the particular case of this research unit or this team.

Criterion 1 - C1 : Scientific outputs and quality ;
Criterion 2 - C2 : Academic reputation and appeal ;
Criterion 3 - C3 : Interactions with the social, economic and cultural environment ;
Criterion 4 - C4 : Organisation and life of the institution (or of the team) ;
Criterion 5 - C5 : Involvement in training through research ;
Criterion 6 - C6 : Strategy and five-year plan.

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

- Grading table of the unit: Cancer Immunity

C1	C2	C3	C4	C5	C6
A+	A+	A	A+	A+	A+

- Grading table of the team: Dendritic cell and T cell biology

C1	C2	C3	C4	C5	C6
A+	A+	A+	NN	NN	A+

- Grading table of the team: Exosomes and tumor growth

C1	C2	C3	C4	C5	C6
A+	A+	A	NN	NN	A+

- Grading table of the team: Cross talk between T cells and dentritic cells

C1	C2	C3	C4	C5	C6
A	A	NN	NN	NN	A+

- Grading table of the team: Spatio-temporal Regulation of Antigen Presentation

C1	C2	C3	C4	C5	C6
A+	A+	NN	NN	NN	A+

- Grading table of the team: Intracellular transport and immunity

C1	C2	C3	C4	C5	C6
A+	A+	NN	NN	NN	A+

- Grading table of the team: Innate like and CD4+ T cells in cancer

C1	C2	C3	C4	C5	C6
A+	A+	A	NN	NN	A+

- Grading table of the team: Integrative Biology of human dendritic cells and T cell

C1	C2	C3	C4	C5	C6
A+	A+	NN	NN	NN	A+

- Grading table of the team: Human innate immunity

C1	C2	C3	C4	C5	C6
A+	A+	NN	NN	NN	A+

Evaluation report

Unit name:	Cancer Immunity
Unit acronym:	
Label requested:	UMR-S
Present no.:	U932
Name of Director (2012-2013):	Mr Sebastian AMIGORENA
Name of Project Leader (2014-2018):	Mr Sebastian AMIGORENA

Expert committee members

Chair:

Ms Muriel MOSER, Free University Brussels, Belgium

Experts:

Mr Vincenzo CERRUNDOLO, Medical Research Council, Oxford, United Kingdom

Mr François GHIRINGELLI, Université de Bourgogne, Dijon (INSERM representative)

Mr Michel GILLIET, Centre Hospitalier Canton de Vaud, Suisse

Mr Günther J. HAMMERLING, Deutsche Krebsforschung Zentrum, Heidelberg, Germany

Mr Hai-Tao HE, Université de la Méditerrannée, Marseille

Mr Vincent PIGUET, Cardiff University, United Kingdom

Mr Willen STOORVOGEL, Utrecht University, The Netherlands

Mr Colin WATTS, Dundee University, United Kingdom

Scientific delegate representing the AERES:

Mr David DOMBROWICZ

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

Mr Daniel LOUVARD, Institut Curie

Ms Stéphanie POMMIER, INSERM

1 • Introduction

History and geographical location of the unit: 26 rue d'Ulm - 75005 Paris

The INSERM Unit 932 is the product of fusion between the two former immunology units at the Institut Curie, U520 and U653, which took place in 2005. Today, the U932 includes 8 teams, located in 3 different buildings.

Management team

The Unit is directed by Mr Sebastian AMIGORENA. All management and strategic decisions are discussed in regular group leader meetings (1-2 times a month), where recruitment (personnel and teams), budget, applications to grants and fellowships are discussed.

In addition, the Unit has a weekly laboratory meeting, in which two staff scientists, students or postdoctoral fellows present the advancement of their project. All teams have additional weekly group meetings. The Unit also organizes a weekly journal club and a yearly retreat and a monthly Immunology Seminar program.

Finally, the "Conseil d'Unité" meets once a year, with all members of the Unit. The director presents the marking events of the past year and the main perspectives for the future, as well as the budget. An open discussion ensues.

AERES nomenclature

SVE1_LS6

Unit workforce

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent researchers from Institutions and similar positions	14	12	12
N3: Other permanent staff (without research duties)	17	14	7
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)			
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	67	23	
N6: Other contractual staff (without research duties)	28	8	
TOTAL N1 to N6	**126**	**57**	**19**

Percentage of producers	***100 %***

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	35	
Theses defended	21	
Postdoctoral students having spent at least 12 months in the unit*	45	
Number of Research Supervisor Qualifications (HDR) taken	8	
Qualified research supervisors (with an HDR) or similar positions	9	11

2 • Assessment of the unit

Strengths and opportunities

Excellent scientific record of the unit; well-thought management; high potential social and economic impact; excellent training; recruitment of young reseachers; original projects of major interest for the next years.

Weaknesses and threats

None (eventually some projects risky or in a highly competitive environment)

Recommendations

The commission was impressed by the quantity and quality of the work of the Unit and advises to simply continue…

3 • Detailed assessments

Assessment of scientific quality and outputs

The work performed and published by the unit represents a major breakthrough in the field of immunology, as assessed by the scientific production (articles published in TOP journals) and the models, tools and methods developped. 149 articles, signed as first or/and last authors by a group leader of the Unit, have been published from 2007-2012 in peer-reviewed journals. 27 articles were published in journals with an impact factor >10 (Nature, Cell, Science, Nat Immunol, Immunity; etc...).

Assessment of the unit's academic reputation and appeal

The Unit has gained an outstanding international reputation in the field of immunology. Researchers of the Unit are regularly invited in international conferences; foreign postdocs are recruited and some teams are leading or participating in international programs. For example, four teams have obtained ERC grants between 2008 and 2011. In 2011, a budget of 1 028 568 EUR was allocated from the European Commission. In 2012, the Unit was granted a Labex (DC-BIOL, where the unit director is one of the 2 co-directors).

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

The Unit has several sustained industrial collaborations and has registered several patents (in the field of cros-presentation, exosomes, HIV innate sensing). In addition, the Unit is involved in Immunology teaching, has organized major conferences, and has participated in the publication of a book. Importantly, the observations of the Unit in basic immunology are likely to be translated to clinical research (cancer, HIV, inflammation) and may have a major impact in medicine. In particular development of new immunotherapies are currently developped in melanoma patients, human psoriasis, HPV infection, HIV; etc... The study of tumor microenvironment should provide new insights in the regulation of tumor resistance *in vivo*.

Assessment of the unit's organisation and life

The philosophy of the Unit concerning the scientific projects of the individual team leaders is a complete freedom and independence. This philosophy promotes risky science and innovative research across disciplines.

The governance appeared excellent, as assessed by the scientific output and the statement by the members of the team themselves. The meeting of subcommittees with directors/students-postdocs/technicians engineers revealed a management recognized as excellent. The technicians/engineers however asked for a better internal communication and would like to be informed about the critical decisions made during team leader meetings.

Common facilities are well organized and fully available, as for example P3 facility, technological platforms and the platform for translational research.

Assessment of the unit's involvement in training through research

The Unit hosts between 10-15 students and 30-35 postdocs. Their training as being part of the Unit includes their participation to laboratory meetings, journal club, yearly retreat and monthly immunology seminars.The students are well integrated in the scientific activities of the Unit, and appeared well guided. The technical platforms are fully available for training and performing experiments.

Assessment of the five-year plan and strategy

The program of all teams was evaluated as ambitious, innovative and of major scientific and medical interest. There is clearly an adequacy between goals and means, in terms of budget, technical competence, availability of equipment and scientific excellence.

Although the philosophy of the Unit is a complete freedom and independence for the individual teams, there is clearly a common scientific interest, creating fruitful collaborations. In addition, the functioning of the Unit relies on the core facilities from the Curie Institute.

Most if not all projects should give rise to major breakthroughs in the field.

4 • Team-by-team analysis

Team 1 : Dendritic cell and T cell biology

Name of team leader: Mr Sebastian AMIGORENA

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	3	3	3
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)			
N6: Other contractual staff (without research duties)	2	2	
TOTAL N1 to N6	**6**	**6**	**4**

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	9	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	3

• Detailed assessments

Assessment of scientific quality and outputs

In the past 5 years the team has published several seminal publications and made several important discoveries providing important insights into the mechanisms controlling cross-presentation, the ability of regulatory T cells in increasing the avidity of primary $CD8^+$ T cells and on the epigenetic control of Th2 differentiation. The team has published 42 articles in the last five years, a high number in top journals (Science, PNAS, Nat Rev Immunol, J. Exp. Med, in 2012).

Assessment of the team academic reputation and appeal

The results obtained demonstrate the breadth and depth of the team leader's research interests and are testimony of his vision, originality and outstanding scientific abilities. He is a world class investigator in the field of DC research and over the years he has made several major contributions in the field of DC biology, Tregs and more recently epigenetic regulation of Th1 and Th2 polarization. The team leader has been invited in in 52 conferences since 2009. The team has attracted numerous postdocs and PhD students (9 postdocs are presently members of the team).

Assessment of the team interaction with the social, economic and cultural environment

The team has filed several patents, which are attracting the interests of several pharmaceutical companies. It is likely that the findings of his basic research will translate into important therapeutic findings.

Assessment of the team organisation and life

See assessment of the unit.

Assessment of the unit's involvement in training through research

See assessment of the unit.

Assessment of the five-year plan and strategy

In the next 5 years, the team will develop two main research programms, which are both an extension of the results and concepts developed by the own team during the past 5 years: 1) antigen cross-presentation by DCs and 2) epigenetic determinants of T cell polarization and memory. The recent discovery of the role of Sec22B in linking the ER to phagosomes will be extended by engineering Sec22b DC conditional knock-out mice to analyse *in vivo* the role of Sec22B in the presentation of microbial and tumour antigens. Experiments will be carried out to dissect the signals and signalling events integrated by DC upon stimulation of different Pattern Recognition Receptors to clarify steps involved in the transport of antigen proteins from lysosomes to the cytosol and in the regulation of phagosome functions during DC maturation. The recent article in Nature published by the group describing the role of H3K9me3/Suv39h/HP1 in Th2 differentiation highlights a previouly unanticipated degree of epigenetic control of adaptive T cell immune responses. It is anticipated that the results of these studies will lead to truely novel discoveries in immunology with diagnostic and therapeutic protential in cancer and inflammatory disorders.

Conclusion

- Strengths and opportunities:

The programme developed by this group is outstanding. The results of the experiments described in the proposal are likely to provide important insights into the role of DC in cross presentation and on the epigenitc control of T cell polarization.

- Weaknesses and threats:

No weaknesses.

- Recommendations:

This is an outstanding programm led by an outstanding scientists, who is a world leader in the field.

Team 2 : Exosomes and tumor growth

Name of team leader: Ms Clotilde THERY

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)		1	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)			
N6: Other contractual staff (without research duties)	1		
TOTAL N1 to N6	**2**	**2**	**2**

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The team leader is a pioneer in the exosome field in which she has been working since 1999, resulting in many publications in high-ranking journals. From 2007 to 2012 she has made remarkable progress in her studies on the cell biology of exosomes, specifically the characterization of the intracellular origin of exosomes and the mechanisms of secretion, and functionalities in immune responses and tumor development. Among others, she has discovered the critical role of Rab27 for exosome secretion (Nature Cell Biol. 2011), but she also found Rab27-independent pathways. It is now realized that cells may release different types of extracellular vesicles with distinct functions on biological processes, as reviewed by the team leader (Nat Rev Immunol 2009).

Previously, there was much enthusiasm about the potential use of tumor exosomes for anti-tumor immunization, among others fostered by a study from the team in which it was shown that tumor-derived exosomes represented a very powerful vaccine, in particular when a tumor antigen was introduced as a fusion protein with the C1C2 domain of MFGE8 lactadherin, a major component in exosomes (Cancer Res 2008). However, by additional elegant work in the team, using tumor cells in which exosome secretion was prevented by Rab27 knock-down, it was found that exosomes could also support tumor progression (Cancer Res. 2012). Thus, the team has contributed to a paradigm shift concerning the clinical use of tumor exosomes. Following this line of research, the team could show a pro-tumor effect of MFGE8 expression in the development of mouse bladder tumors, and also increased MFGE8 expression during human bladder carcinoma progression. Thus, MFGE8 may represent a novel target for therapeutic intervention. Therefore, the team has initiated the production of monoclonal antibodies against MFGE8 together with a biotech company, which are presently being tested for inhibition of human bladder carcinoma in mouse models. Altogether, the research of this 5-year period is original and interesting, with 20 important publications in very good international journals.

Assessment of the team academic reputation and appeal

Ms Clotilde THERY has been working on exosomes since 1998. At this time, exosomes were not widely studied but the pioneering work of the team leader has certainly drawn the attention of other scientists, not only in immunology but also in other areas, with the consequence of an exponentially growing number of publications on this topic ever since, with more than 1300 at this date. The concept that exosomes can provide important modes of intercellular communication is now widely accepted. Other scientists, but also industry, are now investigating the potential of exosomes in body fluids to be used as biomarkers for disease. In 2010, the team leader organized a very successful exosome meeting in Paris at Curie, which was attended by > 200 scientists from all over the world. This was followed by the foundation of the International Society of Extracellular Vesicles (ISEV) by the team leader and others in 2011, of which the team leader was interim vice-chair. Currently, the team leader is the secretary general of the executive board of ISEV. The first annual ISEV meeting was held in Gothenborg in 2012 and counted > 600 participants. The next ISEV meeting is scheduled in 2013 in Boston. ISEV has recently lounched a new journal, the Journal of extracellular vesicles (JEV), of which the team leader is Editor-in-Chief.

Assessment of the team interaction with the social, economic and cultural environment

The studies resulted in filing in 2012 of a patent on new antibodies directed against MFGE8 that decreased tumor cell survival and cell migration.

Assessment of the team organisation and life

See assessment of the unit.

Assessment of the team involvement in training through research

See assessment of the unit.

Assessment of the five-year plan and strategy

In her future project, the team leader plans to continue with her previous line of research, and to concentrate on the role of different types of secreted membrane vesicles and relevant proteins on tumor derived extracellular vesicles in tumor growth and interaction with the immune system. As her work made it clear that more basic research on the biogenesis and diversity in types of extracellular vesicles is required, immunotherapy with exosomes is at present not directly pursued in this laboratory, but 2 clinical phase I/II trials on dendritic cell derived exosomes are ongoing in collaboration with another group.

Subproject 1, Comprehensive cartography of secreted vesicles

As exosomes are heterogenous in size, protein content, and origin, it is planned to isolate more homogenous sub-fractions by differential ultra-centrifugation, density gradients, anion-exchange chromatography, etc. Thereafter, the effect of the different vesicles on immune cells (T cells, APC, NK, Treg, etc.) will be tested. This will be followed by establishment of a quantitative proteomic and RNAomic signature of each vesicle type. Moreover, shRNA will be used to inhibit specifically secretion of particular types of exosomes. This subproject is very interesting from a cell biological and biochemical point of view but it is uncertain whether biochemical separation techniques will yield vesicle fractions which differ according to protein composition, sub-cellular origin, or immune function.

Nevertheless, when successful, it will be of great interest to see how various distinct vesicle populations influence the immune system. Attempts for molecular intervention with the incorporation of relevant cargo into extracellular vesicles (from distinct origin) may also be useful. The spin off from subproject 1 would certainly have additional impact on for the use of extracellular vesicles in subprojects 2/3.

Subproject 2, Relationship between MFGE8 and other alphaVbeta3/5 integrin ligands.

In the context of tumor cell growth and interaction with the immune system, this subproject is directly derived from the team leader's discovery of the pro-tolerogenic properties of MFGE8/lactadherin. The authors plan to analyze the pro-tolerogenic properties also for the human system. In particular, the effect of MFG8 and other αV(3/5 integrin ligands on the tumor microenvironment will be investigated (pro-inflammatory and anti-inflammatory cytokine profiles and cellular sub-populations, eg. M1/M2 macrophages, etc.). This is an interesting project, which may lead to new tumor therapies aiming at inhibiting MFGE8 and other integrin ligands, e.g. with the antibody produced together with a biotech company. The group already showed that MFGE8 is secreted in association with at least two distinct populations of extracellular vesicles, and that rab27a dependent extracellular vesicles (exosomes) from mammary carcinoma cells promoted tumor progression.

Subproject 3, Role of decorin in development of tumors

In the investigation of mouse bladder cancer cell lines, the THERY team has discovered that decorin expression has pro-tumoral effects, similar to expression of MFGE8. Thus, decorin will be analyzed in a way akin to MFGE8, namely effect on the tumor environment, tumor growth, etc., including the production of blocking antibodies against decorin for therapeutic intervention. Also this project is novel and interesting with potential clinical relevance. It could be interesting to investigate vesicles from rab27 depleted cells in relation to decorin.

Altogether, the future projects are original, well founded on previous research, and very promising to provide interesting and novel results.

Conclusion

- Strengths and opportunities:

1. previous work by this group provides a solid foundation of the research plans
2. Original ideas, novel concepts
3. The roles of MFGE8 and decorin in tumor development will be studied, irrespective of their incorporation in tumor exosomes, making subprojects 2/3 independent of succes searched in subproject 1.
4. High international interest/impact
5. Many national and international collaborations

- Weaknesses and threats:

Extracellular vesicles (including exosomes) are multicomponent signalling devices which, due to their complexity, are difficult to study. The observation that multiple types of extracellular vesicles can be formed by the same cell type may complicate studies even further. However, this should not put a brake on this type of investigations. By studying two selected functional components of extracellular vesicles (MFGE8 and decorin) this risk is reduced to a minimum.

- Recommendations:

Continuation of the team work is strongly recommended.

Team 3 : Cross talk between T cells and dentritic cells

Name of team leader: Ms Claire HIVROZ

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)			
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	**2**	**2**	**2**

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

This is a well-established team investigating the early events during T cell receptor signaling and immunological synapse formation. Notably, they were the first to show that the intra-cellular pool of LAT is crucial for initiation of T cell responses. To the biochemical and imaging techniques used so far, the group has recently added a biophysics project aiming at analyzing the biomechanics of the early events of T cell activation upon interaction with antigen-presenting cells. The biomechanics of interaction of immune cells is still an underdeveloped field among immunologists, although it may turn out to become very important and to generate exciting results.

The research projects conducted are divided into three subgroups.

Subproject 1: Analysis of the role of the formation of the immunological synapse (IS) in T cell activation of dendritic cells. Most studies on immune synapse (IS) formation between APC (DC) and T cells concentrate on the role of IS for T cell activation, whereas they have analyzed the role of IS formation for activation of DC by T cells. They could show that IS formation induces modification of the cytoskeleton in DC, leading to increased DC motility, and, thereby, to increased T cell activation. Moreover, in T cells, polarization of MTOC and CD40L is required for induction of IL-12 secretion in DC. However, this is not an absolute requirement. These are new and interesting findings, published in various journals, include one article in *Blood* and two articles in *J Immunol*.

Subproject 2: Biomechanical responses in T cell activation. Based on their finding that IS formation is accompanied by changes in the cytoskeleton, which is important for rigidity/stiffness and motility, the team has employed biophysical approaches in collaboration with UMR 168 (Curie Institute, Paris), to study if the degree of rigidity in APC would influence T cell activation. In a first and very interesting study using artificial model APC the team could show that T cells can sense the biomechanical properties of APC inducing a series of pulling and pushing events in the T cells, the precise force of which can be measured. The associated respective publications include two articles in *PLoS One* and one in *Langmuir*.

Subproject 3: Defective/deregulated activation of pathological T lymphocytes (in collaboration with IMAGINE, Hôpital Necker, Paris). Respective publications include a article in *Eur J Immunol* and several collaborative articles in high profile journals such as *Immunity, Embo J, N Engl J Med, J Allergy Clin Immunol, J Virol…*

Altogether, the work is interesting with an impressive output. There are 16 original publications and reviews, which appeared in the very good journals such as *Blood* and *JI*, and several collaborative articles in high profile journals (Immunity, Embo J, N Engl J Med…).

Assessment of the team's academic reputation and appeal

The team is well-known for its work in the field of TCR signaling and immunological synapse.

The team leader is a member of the Scientific Committee of La Ligue contre le Cancer (2005-2008) and of SIDACTION (since 2009).

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

None reported

Assessment of the team's organisation and life

See assessment of the unit.

Assessment of the team's involvement in training through research

See assessment of the unit.

Assessment of the five-year plan and strategy

In pursuing ongoing studies, the future plan is organized around two main axes: namely the contributions of immunological synapses in T cell signaling, and the role of T cell mechanosensitivity for T cell activation.

The first part of the project is based on the recent observation that VAMP7 SNARE protein can control recruitment and phosphorylation of the vesicular pool of LAT and formation of LAT signalosomes. For their studies, the team employs an impressive combination of molecular silencing approaches and super-resolution fluorescence microscopy. This will be combined with *in vivo* approaches, e.g., testing of the importance of vSNARE VAMP7 *in vivo* using the VAMP7-deficient. mice. This subproject is underway with much progress and a publication on LAT/VAMP7 is presently under revision in *Nature Immunology*.

The second subproject aims at elaborating the importance of biophysical rigidity/stiffness of APC for T cell activation. This project is based on recent observations in other biological systems showing that the mechanical stiffness of stimulatory cells and matrices is of great importance for the biological outcome, including cell migration, proliferation, and apoptosis, and notably also for directed differentiation of stem cells. The studies by the team will be performed in collaboration with a biophysicist from the Institute Curie, who has developed an original custom-made single cell rheometer. The use of this rheometer will give the group an advantage over other immunological groups who are interested in the role of APC rigidity for T cell activation.

Altogether, this is a very original and novel project, adding a new (biophysical) dimension to the mechanism of T cell activation by APC. As at the beginning of this project in vitro experiments will be performed using synthetic matrices of different stiffness, a major issue in the discussions during the site visit was how these *in vitro* studies could be validated *in vivo*. It is hoped that the *in vitro* studies will lead to the definition of molecules /molecular interactions that determine stiffness of a cell, because stiffness must be controlled by molecular events. The identified molecules/biochemical processes may then be used as markers for rigidity of different immune cells at different microenvironments *in vivo*. In conclusion, this is a demanding project entering a new territory, and the results could be very interesting.

Conclusion

- Strengths and opportunities:

Strong collaboration with biophysicists within and outside the Curie Institute, thereby providing the chance for the team to play a leading role in the biomechanics of the interaction of immune cells, a field that is still in its infancy.

The group has obtained original observations on the VAMP7 dependent vesicle trafficking in LAT dynamics and function that can be published well and exploited in future studies.

Excellent environment of the INSERM unit 932

- Weaknesses and threats:

With the biophysics project the group is entering new territory where the outcome is uncertain. It is likely that *in vitro* a contribution of the stiffness of the stimulatory matrix to T cell activation can be observed. However, it will be very challenging to validate and demonstrate such effects *in vivo*, where immune cells are constantly moving through densely packed tissues and lymphoid organs, a process that may be accompanied by constant changes in stiffness. Even if a role for APC rigidity in T cell activation can be shown *in vivo*, it will be very demanding to determine the precise contribution of APC rigidity to antigen presentation in the concert of the many other parameters required for efficient antigen presentation. However, progress in a new field is frequently accompanied by risk.

- Recommendations:

Continuation of the team work is strongly encouraged

Team 4 : Spatio-temporal Regulation of Antigen Presentation

Name of team leader: Ms Ana Maria LENNON

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	2	2	2
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)			
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	**3**	**3**	**3**

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	6	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The stated aim of the group is to 'unravel the fundamental cell biological processes that regulate the life and functions of professional antigen presenting cells'. More specifically they are trying to integrate the basic cell biology of cell migration, endocytosis and receptor signaling via the B cell antigen receptor (BCR) with the events of antigen capture, processing and presentation to T cells. Of course these latter events have been intensively investigated for more than 20 years it can be argued that the immunobiology needs to be better integrated with the cell biology.

Over the past 5 years the group has achieved the above aim in several project areas and in some cases have produced exceptional results. In particular the article published in Science produced the very unexpected and interesting result that the invariant chain chaperone for class II MHC acts as a brake on DC migration so that its destruction alongside antigen processing provides at least part of the signal for DC to migrate. The data were convincing and made biological sense. Several other strong articles focusing on B cells have also been produced. Some extend earlier work from others which showed that convergence of compartments carrying BCR-linked antigen and class II MHC is driven by BCR signaling. The team extended this by showing key roles for Syk and myosin II and provided mechanistic insight by showing that myosin II is linked to the invariant chain. In a more recent study, the team has switched the spotlight to the cell surface of the B cell showing that bead-bound antigen can be extracted by the BCR in a reaction apparently aided by protease secretion and recruitment of cell polarity molecules Cdc42 and atypical PKCξ. The committee feels this was another unexpected and provocative article well supported by the data though not as yet by evidence that these features of antigen extraction occur *in vivo*.

Overall, this relatively recently established team has done extremely well producing at least 2 really novel stories that deservedly were published in the highest ranked journals: Science, as mentioned above, and Immunity (B cell synapse and antigen processing and presentation).

Assessment of the team's academic reputation and appeal

The team leader has been invited speaker at "Keystone Symposium" and "Gordon Conferences".

She received the Gaston Rousseau Prize from the French Academy of Sciences, 2012 and the Olga Sain Prize from the League against Cancer, 2009.

She is the recipient of a "Young Investigator Grant" ERC, 2010-2014.

She is coordinator of the consortium MICEMICO (Cell Migration in Confined Environment) 2009-2013.

She worked as scientific advisor for AERES "life sciences and earth" section, 2010-2011.

She has been advisor of Immunology-Hematology ITMO of Aviesan since 2009.

She is a member of the scientific committee of the Curie institute, 2006-2010 and of the scientific recruitment committee of Paris 7 University, 2006-2009.

Assessment of the team interaction with the social, economic and cultural environment

Interviews for magazines "Research" and "Arte Magazine" in the context of the action of communication "The legacy of Marie Curie."

Participation in the creation and publication of the book "Cell, surprise me" by Editions Berlin, 2007.

Assessment of the team organisation and life

See assessment of the unit.

Assessment of the team involvement in training through research

Organization of three "Summer Schools in Cell Biology" in partnership with the Curie institute and different South American universities.

Participation in the Master II "Membrane Dynamics" at the Paris 5 University.

Assessment of the five-year plan and strategy

The team leader proposes further work in the 2 areas outlined above that have produced the most high profile articles. 1. Co-ordination of antigen presentation and DC migration and 2. The role of cell polarity in antigen presentation in B cells. She sees these areas as highly complementary not least because apparently unpublished data now links different myosin isoforms to the dynamics of the B cell synapse, in other words non-muscle myosin biology is a common theme in both projects.

Medium scale screens are planned to search for new gene products controlling these events which will be followed up eventually at the tissue level. The methodologies/models are multi-disciplinary and at the interface between immunology, cell biology and biophysics, which include among others single molecule imaging, two-photon microscopy, shRNA silencing, transgenic and knock-in animals. These studies will be performed in close collaboration with biologists and physicists/biophysicists both inside and outside the Curie institute.

The team leader wishes to focus on systems biology approaches to identify new genes involved in DC migration and in the formation of the B cell antigen synapse. It was clear from her presentation and subsequent one to one discussions that she will also be following up the immunobiological implications of her very interesting recent studies, particularly the concept of antigen extraction at the B cell synapse. There are many interesting questions that can be addressed here. For example, is there any *in vivo* evidence that B cells create a sealed synapse into which H^+ and proteases can be secreted? How important is this as a mode of antigen processing and capture in vivo? What is the situation when a surface other than a latex bead is used to immobilize antigen and can the need for protease driven extraction of antigen be manipulated depending on the strength of interaction between antigen and the BCR? Also, as was discussed at her lecture, how similar are the synapses that B cells and T cells make with antigen bearing cells and surfaces?.

The team leader gave an excellent presentation and plans to address these issues alongside shRNA screens for new gene products that control cell polarity and migration. Overall, this is a strong, ambitious and feasible research program.

Conclusion

- Strengths and opportunities

The team leader has a clear ability to formulate new concepts and is able to co-ordinate the experimental programmes needed to test them. Her work is highly interdisciplinary synchronizing studies between immunology, cell biology and biophysics. She is able to see a 'big picture' and to see connections between cellular events that are not obvious. This is impressive in someone who is still at a relatively early stage in her career. She also has strong national and international collaborations with the best experts in the fields.

- Weaknesses and threats

The committee does not feel there are any significant issues.

- Recommendations

Continuation of the team work is strongly recommended.

Team 5 : Intracellular transport and immunity

Name of team leader: Mr Philippe BENAROCH

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)			
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	**2**	**2**	**2**

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	4	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The team has continued its main focus on the cell biology of HIV, its interface with the endocytic pathway and more general aspects of virus interaction with the immune system. The team's approach reflects the leader's background in protein and vesicle 'trafficking' and makes extensive use of light and electron microscopy, knockdown strategies, co-immuno-precipitation etc. A very attractive feature of the team's recent work is a general aversion to using cell lines and a willingness to 'go the extra mile' and conduct experiments in more technically challenging primary cell systems, including primary human cells. This gives them a distinct edge and identity in the competitive areas they work in.

The team recent output is not huge but is of high quality: 15 publications in very good to excellent international journals (Cell Host & Microbe, J Cell Biol, PNAS, Blood) during the last 5 years.. A look back at the group's publications from the previous 5 year period (2002-2007) suggests that it has reached a higher level since 2007 and has addressed more substantive issues. This is reflected in the journals it has published in. In some cases, its use of primary human cells has probably limited the range of experiments possible (and perhaps the target Journal) compared with the more manipulable mouse system. For example, the work on MHC class II trafficking in plasmacytoid dendritic cells (pDCs) published in Blood reported very similar results to their competitors, who, working with murine pDC managed to publish in Nature Immunology with a bit more data. New projects have been started for example the study on TLR3 processing and trafficking. This again produced an article in a good journal.

Assessment of the team's academic reputation and appeal

The group leader has been invited to a number of conferences including a Gordon conference and an International workshop on Antigen Presentation as well as several conferences on retroviruses and macrophages.

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

The team has filed 2 patents regarding potential HIV infection treatment in 2010 and 2012.

Assessment of the team organisation and life

See assessment of the unit.

Assessment of the team involvement in training through research

See assessment of the unit.

Assessment of the five-year plan and strategy

The team leader plans 2 main areas for development over the next 5 years.

First, the team plans to continue studies on Toll like receptor 3 (TLR3) trafficking and signaling. In part these studies will compare TLR3 in different human and mouse DC sub-types. They also plan to take advantage of a new technology developed by Institut Curie colleagues that allows synchronized release of proteins from the endoplasmic reticulum. Preliminary data shows that this will allow a kinetic analysis of TLR transport, processing and the acquisition of signaling function to be studied alongside imaging studies. The aim is to determine when TLR3 becomes competent to signal and whether different signals emanate from different compartments, though this could be challenging to establish. A number of groups are working on TLRs such as TLR3 that signal from the endocytic pathway so this is a very competitive area. Nonetheless, the use of this novel technology should allow the group to maintain an edge in this area.

The second area to be continued is the cell biology of HIV assembly, transport and release from macrophages. The team has been instrumental in demonstrating the important role of macrophages as viral reservoirs in HIV infection and has characterized intracellular compartments where new virions are assembled. Very interestingly, the team recently generated new data indicating that the scavenger receptor CD36 may be crucial to the biogenesis and/or stability of this compartment which appears to be distinct to conventional endosomes. Knockdown of CD36 or exposure to anti-CD36 antibodies suppresses release of new HIV virions so CD36 could be a novel target for anti-retroviral therapy. A patent on this subject has been filed. A variety of tools including 2-hybrid libraries, antibodies and various mutants of CD36 are under construction to permit full exploitation of this potentially important finding. Again, this is obviously a competitive area but the group is well established in it and has plenty of interesting new data.

Conclusion

- Strengths and opportunities

The group leader has a strong background in cell biology which gives him a distinct perspective on the virological and immunological questions he is addressing. He has embraced and indeed runs some of the technology platforms at the Institut Curie which again gives him a competitive advantage. His focus on and experience in working with primary cells also sets him apart from many other groups who use cell lines. Overall, the quality of the projects and the wider scientific environment should ensure continued productivity and innovative science.

- Weaknesses and threats

The team is working in very competitive areas: TLR signalling and HIV so inevitably there is a risk that other groups may publish first in key areas. As outlined above, it has some new technologies and more importantly, preliminary data that should ensure their competitiveness.

- Recommendations

The committee recommends to continue the current work

Team 6 : Innate like and CD4+ T cells in cancer

Name of team leader: Mr Olivier LANTZ

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	2	2	2
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)			
N6: Other contractual staff (without research duties)	1	1	
TOTAL N1 to N6	**4**	**4**	**3**

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the unit	5	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The team develops 3 research themes. After the seminal article published in Nature describing the role of MR1 for the activation of MAIT cells by the commensal flora, the group has published a steady string of articles characterizing the development and specificity of MAIT cells and in 2010 demonstrated the ability of MAIT cells to recognized bacteria infected cells. Generation of MAIT TCR transgenic mice has allowed to study the role of MR1 in the positive selection of MAIT cells. In addition to this program, this group has continued to develop a tumor immunology program. Experiments in mice revealed a high mortality due to a cytokine storm possibly related to the ability of long peptide to be presented by B cells. The team is the international leader of this small field of immunology.

The committee observes a very strong expertise in the field of CD4 T cell biology, in the capacity to generate very innovative and difficult animal models to answer to mechanistic problems. The team developed tools for studying MAIT cells. These tools are unique in the world and will give major insight in the biology of this cells population. During the last 5 years, this group has published 25 articles in very good to excellent high impact factor international journals (Blood, Plos Biology, PNAS, Nature Immunology). Altogether, the scientific output of the team is excellent. The financial support is excellent.

Assessment of the team's academic reputation and appeal

The team leader is well recognized in the field of fundamental immunology especially in the field of tumor vaccine, MAIT cells and CD4 T cell responses. Altogether, the scientific reputation of the team is excellent. The team leader has been invited in 8 international meetings since 2008.

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

The team is currently developing translational programs in melanoma patients, which may provide important finding for future clinical trials.

Assessment of the team's organisation and life

See assessment of the unit

Assessment of the team's involvement in training through research

See assessment of the unit.

Assessment of the five-year plan and strategy

The program is divided in 3 themes:

1. The major part of the work focuses on MAIT cells and follows the previous results published in the last 5 years. The team will study the ontogeny of MAIT cells using B6/cast mice. The objective will be to determine how MAIT cells acquire their specific features in the thymus and to identify the cells that trigger their differentiation. Then the team will study the biology of MAIT in the periphery and determine how interactions between B cells, bacteria and MAIT drive their proliferation and activation. Then the team will search for the specific master transcriptional factor(s) of MAIT and try to generate MAIT tag mice. Finally, in human the team will search whether some populations are deficient in MAIT and search for a clinical relevance of this observation.

The second part of the program on MAIT is the characterization of MAIT cell ligand from bacteria using biochemical and genetic approaches.

The third part of this theme is to study the functions of MAIT cells. The team will focus on context dependent activation in in vitro model of MAIT activation; then analyze their role in the control of bacterial infections and in the context of BCG therapy in bladder cancer.

2. The second theme involves tumor immunology and consists in the generation of a model of spontaneous tumor with a dominant antigen expressed only in the cancer cells.

3. The third theme aims at developing new cancer vaccine. The idea is to associate long peptide with MAIT ligand to test whether this complex may enhance tumor immunity.

The committee considers the program focus on MAIT cell an exciting and novel chapter in Immunology and the Lantz team will certainly be amongst those groups that will significantly contribute to the field. The BCG project in bladder cancer patients, linked to the analysis of MAIT cells in the blood and urine is an exciting program which may provide insight into the therapeutic properties of BCG treatment in bladder cancer patients. A clinical trial is also planned to assess the ability of long peptides to elicit an immune response in melanoma patients in the presence of CpG, NKT cells agonist and MAIT cell agonist.

Conclusion

- Strengths and opportunities:

The committee notes the regular recruitment of post doctoral fellows and the large financial support from funding boardings. The expertise in the field is exceptional. The work on MAIT cells will lead to important fundamental discovery.

- Weaknesses and threats:

None.

- Recommendations:

The committee recommends to continue the current work.

Team 7 : Integrative Biology of human dendritic cells and T cell

Name of team leader: Mr Vassili SOUMELIS

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)	1	1	1
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)			
N6: Other contractual staff (without research duties)	2	2	
TOTAL N1 to N6	**4**	**4**	**2**

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit	6	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The focus of the team is dendritic cell biology. The team developed a strong expertise in the field of human dendritic cells biology, in particular on plasmacytoid dendritic cells. The team leader discovered the key function of TSLP and is continuing to work on this with an international reputation. The group has now moved toward a more integrative approach using a systems biology approach. The publication track-record of the team, the financial support, and the international recognition are excellent. The team has published 24 articles in very good to excellent (Blood, Nature Immunology, J. Exp. Med.) international journals in the last five years. The team leader has been invited in 6 international conferences.

During the past 5 years, the team leader has developed a new line of research based on computational data integration. The team can take advantage of the local infrastructure and the integrative biology program provided by the Institute. The team leader is also a hemato-oncologist in the Curie Hospital. This activity favours the excellent collaboration with the clinic and his research on the tumor microenvironment development of immunotherapy trials. Alltogether, the scientific output of the team is excellent.

Assessment of the team academic reputation and appeal

The team leader has a undisputed reputation as the discoverer of TSLP function in 2001. As a postdoctoral fellow, he discovered the role of pDC in adaptive immunity (Science) and the role of TSLP in driving DC-mediated allergic T cell responses (Nature Immunology). As an independent investigator in the Unit since 2004, he has continued to work on these topics very successfully with several high impact publications, including J. Exp. Med., Nature, Nature Immunology. This discovery has generated an entire research field and TSLP is now being developped as a therapeutic for allergic asthma and atopic dermatitis.

The team leader is also recognized as an international expert in DC biology and is regularly invited to international meetings on the topic (such as Keystone meetings). The team leader has been invited in 6 international conferences. Altogether, the reputation of the team is excellent.

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

The team leader is hematologist with half day clinic a day. His research activity involves immunotherapeutic clinical trials aiming at directly testing and improving patient's life.

Assessment of the team's organisation and life

See assessment of the unit.

Assessment of the team's involvement in training through research

See assessment of the unit.

Assessment of the five-year plan and strategy

The program is divided in 3 parts:

1. The use of mathematic modeling to analyze large scale data and perform the subsequent experimental validation. The work is based on transcriptomic profiling. The objectives are to determine how DC and T cells integrate combination of signal such as TLR signal and other cell signals.

2. The role of TSLP in immune biology. The team will look at the role of TSLP in DC migration, the role of TSLPR (function and downstream pathway. The team will also determine molecules involve in the production of TSLP and the prognostic ole of TSLP in cancer setting.

3. Characterisation of tumor microenvironment in the context of head and neck and breast cancer will be performed. This work focuses on cross talk between DC and cancer cells and will be based on integrative biology with large transcriptomic analysis.

This an ambitious, innovative research project which has a high potential for translational research.

Conclusion

- Strengths and opportunities:

The use of bioinformatic strategy to answer to biological question and the possibility to perform some multiple large scale analysis on patients with breast cancer is a very innovative and unique strategy that may lead to new and important discoveries. The team leader has shown the ability to acquire a large amount of funding for his research and to publish high-impact articles.

- Weaknesses and threats:

The work on multimodal integration of signals is vast and high risk. In particular, it seems challenging to use these data to model in-vivo biological processes. However, the team leader has already shown feasibility of his systems biology approaches with some high-impact publications such as Nature Immunology. Furthermore, the team leader has created a network of bioinformaticians and mathematicians to support his work.

- Recommendations:

We highly recommend the team leader to continue his work. The high-risk but innovative work on integrative biology and the well-established work on pDC and TSLP are a good combination to guarantee the continued success of the team.

Team 8 : Human innate immunity

Name of team leader: Mr Nicolas MANEL

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions			
N2: Permanent EPST or EPIC researchers and similar positions	1	1	1
N3: Other permanent staff (without research duties)			
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)			
N6: Other contractual staff (without research duties)	2	1	1
TOTAL N1 to N6	**3**	**2**	**2**

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended		
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The team leaderl has past contributions for a junior scientist which are of very high calibre with a recent Nature publication that was obtained during his post-doctoral time in the US. He also successfully obtained an ERC grant which is prestigious since his return in France. Since he has been in the Curie Institute, he has already produced new results that can lead to high impact publications in a short period of time. He has already enough results for two future publications of excellent quality. Overall the committee ranks the scientific output as excellent based on his postdoctoral time in the USA.

Assessment of the team academic reputation and appeal

The scientific reputation of the team leader in the field of HIV is already strong and he is likely to become a future leader in this area. At his stage, not all junior scientists have already achieved recognition in the international research community. This is of course early to extensively comment on this as he may need several years to be well-established.

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

The team leader has filed a patent as a result of his basic science and recent results. He also extends his basic research into transnational research that can benefit patients. Finally he is studying HIV-2 infection which is an area of unmet needs and has been understudied and represents probably a neglected tropical disease.

Assessment of the team's organisation and life

Not applicable.

Assessment of the team involvement in training through research

See assessment of the unit.

Assessment of the five-year plan and strategy

The team leader's future projects are promising, based on his recent results in particular on the cryptic innate response to HIV-1 in DC. We are confident that his research programme will be successful and lead to additional scientific discoveries and high profile publications. His projects are clear and well designed and composed of a good portfolio of high risk and medium risk projects.

Conclusion

● Strengths and opportunities:

The team leader is a bright new investigator and should make significant contributions to his scientific field in the coming years. He has already impressive publications and new data. He is currently well funded which will help him to develop his research on this competitive topic. He has also an excellent environment to succeed in his future projects.

● Weaknesses and threats:

The team leader works on a very competitive topic and will need to make significant progresses with his projects to achieve high impact publications.

● Recommendations:

Continue the excellent work.

5 • Conduct of the visit

Visit dates:

Start: January 24th, 2013

End: January 25th, 2013

Visit site: Institut Curie

Institution: Inserm, Institut Curie

Address: 26, rue d'Ulm 75248 Paris Cedex 05

Conduct or programme of visit:

Jeudi 24 janvier			
9h - 9h10	Accueil du comité	Mr Sebastian AMIGORENA Mr Daniel LOUVARD	Salle Joliot Curie
9h10 - 09h30	Réunion comité huis clos	Membre du comité	Salle Joliot Curie
9h30 - 9h40	Présentation des membres du jury et Rappel sur le rôle et la procédure d'évaluation	all U932	Amphi Marie Curie
9h40 - 10h35	Présentation du Bilan de du Projet de l'Unité par Sebastian AMIGORENA	all U932	Amphi Marie Curie
10h35 - 10h 50	Pause		Salle Joliot Curie
10h50 - 11h45	Présentation Team 1 AMIGORENA : Dendritic cell and T cell biology	Equipe Mr Sebastian AMIGORENA	Amphi Marie Curie
11h45 - 12h35	Présentation Team 2 THÉRY : Exosomes and tumor growth	Equipe Ms Clotilde THERY	Amphi Marie Curie
12h35 - 13h45	Déjeuner - Session poster batiment Pasteur	comité + étudiant	Entresol
13h45 - 14h35	Présentation Team 3 HIVROZ : Cross talk between T cells and dentritic cells	Equipe Ms Claire HIVROZ	Amphi Marie Curie
14h45 - 15h25	Présentation Team 4 LENNON : Spatio-temporal Regulation of Antigen Presentation	Equipe Ms Ana Maria LENNON	Amphi Marie Curie
15h25 - 15h40	Pause		Salle Joliot Curie
15h40 - 16h20	Présentation Team 5 BENAROCH : Intracellular transport and immunity	Equipe Mr Philippe BENAROCH	Amphi Marie Curie
16h20 - 17h10	Présentation Team 6 LANTZ : Innate like and CD4+ T cells in cancer	Equipe Mr Olivier LANTZ	Amphi Marie Curie
17h10	Réunion comité huis clos	Membre du comité	Salle Joliot Curie
Vendredi 25 janvier			
9h - 9h50	Présentation Team 7 SOUMELIS : Integrative Biology of human dendritic cells and T cell	Equipe Mr Vassili SOUMELIS	Amphi Marie Curie
9h50 - 10h40	Présentation Team 8 MANEL : Human innate immunity	Equipe Mr Nicolas MANEL	Amphi Marie Curie
10h40 - 10h 55	Pause		Salle Joliot Curie
10h55 - 11h15	Rencontre du comité avec les représentants des tutelles "officielles" de l'unité: Inserm et Institut Curie	Daniel Mr LOUVARD (Inserm à préciser)	Salle Joliot Curie
11h15 - 11h50	Entretiens avec les chercheurs et enseignants-chercheurs	Chercheurs	Salle Joliot Curie
	Entretiens avec les étudiants et post-doctorants	Etudiants + Post doc	Amphi Marie Curie
	Entretiens avec les ITA	ITA	Chez Marie
11h50 - 13h15	Déjeuner - session poster bat Lhomond et Hôpital		Chez Marie
13h15 - 17h	Réunion à huis clos du comité	Membres du comité	Salle Joliot Curie

Specific points to be mentioned:

The entire review committee attended all presentations and discussions of the team leaders. Each 25 min presentation was followed by 20 min discussion.

The review committee was then split into three subcommittees in order to meet (1) the staff scientists, (2) the students and postdocs and (3) the technicians and engineers.

6 • Statistics by field: SVE on 10/06/2013

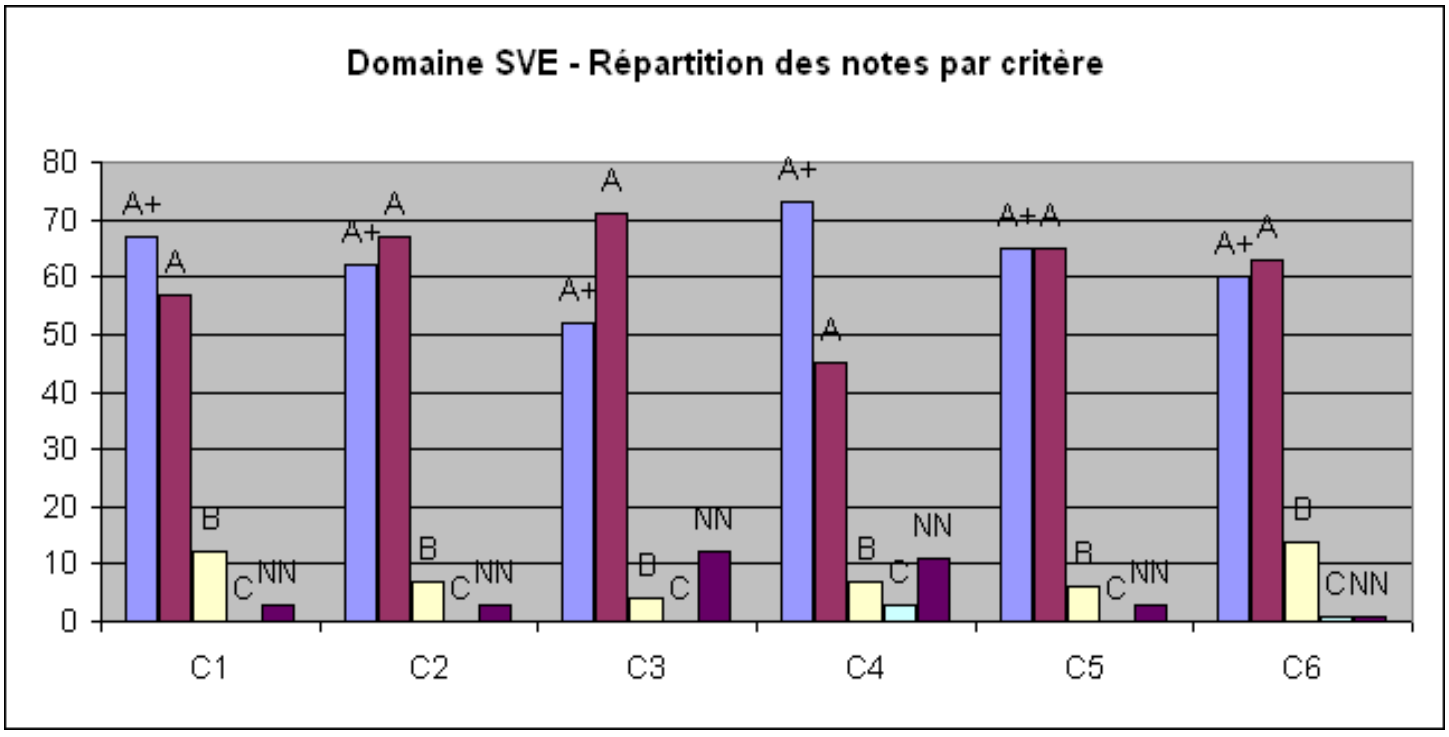
Grades

Critères	C1 Qualité scientifique et production	C2 Rayonnement et attractivité académiques	C3 Relations avec l'environnement social, économique et culturel	C4 Organisation et vie de l'entité	C5 Implication dans la formation par la recherche	C6 Stratégie et projet à cinq ans
A+	67	62	52	73	65	60
A	57	67	71	45	65	63
B	12	7	4	7	6	14
C	0	0	0	3	0	1
Non Noté	3	3	12	11	3	1

Percentages

Critères	C1 Qualité scientifique et production	C2 Rayonnement et attractivité académiques	C3 Relations avec l'environnement social, économique et culturel	C4 Organisation et vie de l'entité	C5 Implication dans la formation par la recherche	C6 Stratégie et projet à cinq ans
A+	48%	45%	37%	53%	47%	43%
A	41%	48%	51%	32%	47%	45%
B	9%	5%	3%	5%	4%	10%
C	0%	0%	0%	2%	0%	1%
Non Noté	2%	2%	9%	8%	2%	1%

Histogram



7 • Supervising bodies' general comments

CENTRE DE RECHERCHE

institutCurie
Ensemble, prenons le cancer de vitesse.

AERES
Section des Unités
20, rue Vivienne
75002 PARIS

Paris, le 17 avril 2013

Concerne : Rapport : S2PUR140006165 - Immunité et Cancer - 0753172R
Unité IC/INSERM U932 : Directeur : Sebastian Amigorena

Chers Collègues,

En tant qu'organisme hébergeur et déposant unique des rapports des unités de recherche du site de Paris de l'Institut Curie – Vague D, je vous informe avoir bien reçu en date du 29 Mars dernier, le rapport d'évaluation de l'AERES sur l'unité IC/INSERM U932.

Je n'ai pas d'observation à apporter au document qui nous a été fourni. Je tiens à saluer le travail réalisé par les experts.

Afin d'assurer le succès continu de cette unité, j'ai bien noté les recommandations du comité pour appuyer ce plan en tenant compte de l'évolution de cette unité et tous les efforts seront faits en coordination avec les tutelles : l'Institut Curie et l'INSERM et notre partenaire l'Université Paris Descartes (Paris 5) pour assurer les soutiens nécessaires.

Je tiens à exprimer tous mes remerciements aux membres du comité d'évaluation pour leurs commentaires et recommandations très pertinents qui sont basés sur un travail d'analyse approfondie. Je remercie également l'équipe de l'AERES qui a soutenu la mise en oeuvre de l'ensemble de cette évaluation.

Je vous prie d'accepter, Chers Collègues, mes plus cordiales salutations.

INSTITUT CURIE SECTION RECHERCHE

Daniel LOUVARD
Directeur de la Section de Recherche
INSTITUT CURIE

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