Recherche clinique appliquée à l'hématologie

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on unit:

Clinical research in hematology, immunology and transplantation

Under the supervision of the following institutions and research bodies:

University Paris 7- Denis Diderot

January 2013

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

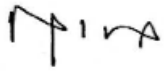
Research Units Department

President of AERES

Didier Houssin

Research Units Department

Department Head



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: Clinical research in hematology, immunology and transplantation

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

- Grading table of the team: Acute Leukemias

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

- Grading table of the team: Aplastic anemia and hereditary blood disorders

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

- Grading table of the team: HSCT

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

- Grading table of the team: Adult primary immune deficiencies

C1	C2	C3	C4	C5	C6
A	*A*	*A*	*NN*	*B*	*A*

Evaluation report

Unit name:	Clinical research in hematology, immunology and transplantation
Unit acronym:	
Label requested:	EA
Present no.:	EA3518
Name of Director (2012-2013):	Mr Hervé DOMBRET
Name of Project Leader (2014-2018):	Mr Hervé DOMBRET

Expert committee members

Chair: Mr Philippe MOREAU, CHU Nantes

Experts:

Mr Alan BURNETT, University of Cardiff, United Kingdom

Mr Jean-Yves CAHN, University Hospital of Grenoble (representative of CNU)

Mr Charles DUMONTET, Léon Bérard Center

Mr Thierry Lamy DE LA CHAPELLE, University of Rennes

Mr André TICHELLI, University Hospital of Basel, Switzerland

Scientific delegate representing the AERES:

Ms Sophie DE BENTZMANN

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

Mr Benoit SCHLEMMER, University Paris 7

1 • Introduction

History and geographical location of the unit

The unit EA3518 was created in 2001 by Ms Eliane GLUCKMAN (initially referenced as EA1814). The team was originally devoted to clinical research in allogeneic hematopoietic stem cell transplantation (HSCT) and Fanconi anemia (FA). Mr Hervé DOMBRET became the head in 2005 and a second team dedicated to clinical research on acute leukemia (both acute myeloid leukemia [AML] and acute lymphoblastic leukemia [ALL]) had been added. Upon last AERES evaluation done on February 2008, the EA3518 was thus restructured during the 2008-2012 period, into four distinct themes: i) Theme 1: Acute Leukemias; ii) Theme 2: Bone Marrow Failures; iii) Theme 3: HSCT; and iv) Theme 4: Adult Primary Immune Deficiencies. More recently, a new Leukemia Translational Lab (LTL) was created in February 2012 by the acute leukemia axis. This LTL, devoted to public/private partnerships for preclinical and early clinical studies evaluating new anti-leukemic agents, has been funded in 2011 by the first investment plan (Investissements d'Avenir, Projet IHU) and by fundings from the Agence Nationale de la Recherche (ANR). The unit is composed of subgroups working mainly at Hospital St Louis (IUH) and Hospital Robert Debré.

Management team

Mr Hervé DOMBRET is the director of EA3518.

Unit workforce

Overall, the unit hosts 7 teacher-researchers (including 4 Professors [PU-PH], 1 Lecturer [MCUPH] and 2 Assistants [CCA/AHU]), 1 retired emerite Professor, 3 full-time researchers, and 12 part-time researchers (including 10 Medical Practitioners [PH]). The unit also hosts 17 technicians, engineers, or administrative persons (15 at full-time).

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	4	4	4
N2: Permanent researchers from Institutions and similar positions	3	3	3
N3: Other permanent staff (without research duties)	17	17	17
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)	1	1	1
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	12	12	12
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	37	37	37

Percentage of producers	***100%***

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	0	
Postdoctoral students having spent at least 12 months in the unit*	1	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	7	7

2. Assessment of the unit

Strengths and opportunities

The unit EA3518 includes 4 different teams. The team coordinators are all international experts in their field. The number of patients treated in Saint-Louis hospital is very high, favoring the recruitment of large numbers of cases for each team. Team 2 and Team 4 are capturing the majority of French cases in their field. The LTL is opening a new window of opportunity for translational research. The strategy of Saint-Louis hospital, IUH and University Paris Diderot is consensual , in order to favor the development of clinical and translational research. The future arrival of an eminent specialist in myelodysplastic syndromes is likely to enhance the overall activity.

Weaknesses and threats

- The unit is situated in 5 different locations, with few real connections between teams.
- The teams are too independent, without any formal meeting involving all 4 teams.
- Two teams, although excellent, have potential vulnerability: team 3 within which Eurocord Registry, which relies mainly on an emeritus professor, has a major issue with respect to future long-term planning and durable funding following his departure; team 4, that relies mainly on one PU-PH, needs to be consolidated with other collaborators.
- The LTL is promising, but will rely in the future on a single physician, who is also responsible for significant and time-consuming clinical activities performed outside the IUH.
- The strategy of including an eminent specialist in myelodysplasia syndromes and his collaborators into the EA3518 is not clearly defined.
- There is a high risk of competition with another group in Paris working on some identical topics.
- The central management of the whole unit to coordinate available resources and strategies is poor.

Recommendations

- The committee underlines that the management of the 4 teams has to be improved by creating structured regular management, meetings and collaborations.
- A strategical effort has to be made to solve the long-term strategy for the team 3, especially to maintain the Eurocord leadership within the unit.
- The translational leukaemia (LTL) lab has to develop strategies to attract at least one full-time scientist.
- Team 4 has a critical size and has to attract new collaborators.
- Collaborations with teams working in IUH in basic science have undoubtedly to be reinforced more clearly.
- Future collaborations with eminents specialists in myeloproliferative disorders, and the INCa-supported Clinical Investigation Center, respectively have to be established.

3. Detailed assessments

Assessment of scientific quality and outputs

Over the last 4 years, the EA3518 unit produced a high number of excellent publications, showing its capacity of valorization of clinical and bio-clinical cohorts of patients. The scientific work has a relevant impact not only at the national but also at the international level The scientific quality of the publications is particularly high and original with high impact factors as detailed team by team. A significant number of publications relies on unique ressources in the field of bone marrow failures, hematopoietic stem cell transplantation, or adult primary immune deficiencies.

Assessment of the unit's academic reputation and appeal

The EA3518 unit is a unique structure in France. It represents the reference centre in France for some rare diseases, in addition with the unique Eurocord organization. The reputation of its team coordinators is not limited to France since they are internationally visible and recognized and are frequently invited as speakers in international meetings. Despite its leadership and renown, the EA3518 unit has difficulties in recruiting PhDs.

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

The main social impact of some teams of the EA3518 unit is their strong interactions and active involvement within the specific patients' groups for rare diseases (especially Team 2 and Team 4). Team coordinators are strongly involved in structured teaching and information meetings for the patients and their relatives, and have active interactions with the patients' organizations at the national and international levels.

Assessment of the unit's organisation and life

The four teams are working independently. Moreover, they are located in 5 different buildings/areas, a point which is not favoring interactions and ressource optimizing. Tasks are well-defined within each team, but few or no global meetings are organized. The role of the director should be reinforced to integrate the different projects of each team. Formal meetings with team coordinatorshave also to be systematically organized. The overall strategy is lacking collective discussions with team coordinators.

Assessment of the unit's involvement in training through research

Overall, the EA3518 unit is continuously training students, assistants and residents who are enjoying the unique opportunity to learn and to make research on rare diseases. Importantly, the team coordinators give to the young training researchers the opportunity to report on studies at high level national and international meetings (ASH, EHA, EBMT annual meetings). Team coordinators are systematically proposing studies to be published by young investigators, who are involved as first author in these publications. Projects being based on access to collaborative groups' databases to address specific questions, this conveniently provides young investigators with projects (and therefore research training) to pursue. Furthermore, the team coordinators are actively involved in teaching hematology, within the hospital, and also at the national and international levels. They are participating in the elaboration of national and international guidelines. Nevertheless, so far there is no unit-wide structured training program for doctoral students and MD-PhD.

Assessment of the five-year plan and strategy

The overall strategy should be more clearly defined. The integration of new diseases and investigators (MDS, myeloproliferative diseases) should be clarified. The activity of the LTL should be prioritized. The connections with the labs working on basic science should be promoted.

4 • Team-by-team analysis

Team 1 : Acute Leukemias

Name of team leader: Mr Hervé DOMBRET and Mr André BARUCHEL

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	4	4	4
N2: Permanent EPST or EPIC researchers and similar positions	2	2	2
N3: Other permanent staff (without research duties)	4	4	4
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1	1
N6: Other contractual staff (without research duties)	6	6	6
TOTAL N1 to N6	17	17	17

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	0	
Postdoctoral students having spent at least 12 months in the unit	0	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	4	4

• Detailed assessments

Assessment of scientific quality and outputs

This team has led to publications in high level journals such as in Blood, J Clin Oncology, Lancet, Bone marrow transplant, New England J Med, Leukemia, Curr opin in haematology.. Overall, the published scientific work is excellent, with a significant impact not only at the national but also at the international levels.

Assessment of the unit's academic reputation and appeal

This team is co-coordinated by two specialists for adult acute myeloid leukaemia (AML) and for paediatric acute lymphoblastic leukaemia (ALL), who are international leaders in these diseases and lead the French collaborative groups, ALFA and FRALLE, respectively. They are invited speakers in international conferences in their fields on a regular basis.

Assessment of the unit's organisation and life

The responsabilities and the tasks are well-defined. The recruitment is very important. Nevertheless, a stronger interaction between the team staff and basic research and translational groups is needed.

Assessment of the unit's involvement in training through research

Members of this team are frequently training students, fellows and residents. The permanent members are also allowing young researchers in training to present studies at national and international meetings, such as ASH or EHA. Young investigators may be involved as first authors in publications.

Members involved are also actively involved in teaching of hematology at the local, national and international levels.

Nevertheless, there is no structured training program for doctoral students or MD-PhDs, and consequently, few candidates to integrate the group.

Assessment of the five-year plan and strategy

The 5-year plan and strategy is based on access to collaborative groups' databases to address specific questions. The collaboration between adult and paediatric clinical services created the Adolescent and Young Adults as a separate entity, that will allow the development of specific programs focusing on quality of life, social and perhaps fertility and long-term consequences of treatment in this group. A translational component corresponding to the LTL is an important emerging aspect.

Conclusions

- Strengths and opportunities:

This team is co-coordinated by two specialists for adult acute myeloid leukaemia (AML) and for paediatric acute lymphoblastic leukaemia (ALL), who are international leaders in these diseases and lead the French collaborative groups, ALFA and FRALLE, respectively. There is a very large leukaemia service in the Hospital Saint Louis which provides the clinical databases as well as represents a source of clinical samples for translational research.

The strategy is based on access to collaborative groups' databases to address specific questions. This is carried out with strong statistical support coming from a researcher belonging to another unit located outside the site. Despite this, this collaboration works well. The projects include: i) the identification of which older AML patients who should not be subjected to intensive chemotherapy. ii) a “cure” model for older AML patients, iii) the adoption of Mantyl Byar methodology to assess the role of transplant in AML patients with adverse risk cytogenetics, and iv) a detailed study on Sweet syndrome. All of these studies have led to publications or presentations. Other projects are ongoing.

The pediatric ALL strategy is similar, although adopting more international collaborations because of fewer patients. The projects include the consequences of induction failure, anthracycline dosing and a number of other studies highly influenced by Dr Baruchel though international collaboration. These published studies increase the already very strong publication output from staff involved in Team 1 through leadership of the ALFA and FRALLE Groups.

The strong collaboration between adult and pediatric clinical services is unusual and has borne fruit with the development the Adolescent and Young Adults as a separate entity. This provides an opportunity particularly under the heading of quality of life, social and perhaps fertility and long-term consequences of treatment in this group. There is also a strong interaction with the transplant service and Team3.

Although presented as a purely clinical research programme, a translational component corresponding to the LTL is an important emerging aspect. This has been locally recognized and recently (2012) implemented with the appointment of 2 laboratory technician positions to develop a system for *in vitro* (and possibly *in vivo*) assessment of new therapeutical agents. This will achieve a number of important benefits for the unit. First, it will add a scientific lab component which could well develop into a fertile niche for students. While this is a benefit, it also brings obligations with respect to training and career development of the scientific staff. Second, it is likely that new scientific opportunities will emerge which will require access to the technical ressources already in place on the campus. While this may be assisted by further collaborations, it is likely that the structure has to attract a full-time scientist to take this group forward. Third it will pave the way for developing early stage trials of these agents either in-house or by collaborations, which could eventually be taken forward to the respective Collaborative Group portfolio. This activity could represent a rewarding opportunity for Partnership funding from industry.

Apart from the clearly expressed aim to develop the LTL, it is likely that other aims are being considered, but these need to be more clearly formulated.

- Weaknesses and threats:
  - A stronger interaction between the team staff and basic research and translational groups would enhance activity and development and is recommended exploiting when possible available platforms (either in Saint Louis or elsewhere).
  - A more active participation in training programmes has to be be considered.
  - To fully develop the translational laboratory, additional resources will be required but represent a unique opportunity to attract research or pharmaceutical grants.
- Recommendations:

Given that team coordinators are senior experts, it is considered important to consider where future leadership of this important component of the unit will come from in 5 to 10 years time. To fully develop the translational laboratory additional resources will be required which will require research or pharmaceutical grants.

Team 2: Aplastic anemia and hereditary blood disorders

Name of team leader: Mr Thierry LEBLANC

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			
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)	3	3	3
TOTAL N1 to N6	4	4	4

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	0	
Theses defended	0	
Postdoctoral students having spent at least 12 months in the unit	0	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	0	0

• Detailed assessments

The team 2 covers mainly two axes, the inherited bone marrow failure (IBMF), and the acquired BMF, including aplastic anemia as well as paroxysmal nocturnal hemoglobinuria (PNH).

Assessment of scientific quality and outputs

Because IBMFs are rare diseases, and the diagnoses are performed nearly exclusively in specialized laboratories in connection with the team, team 2 covers a complete and large database including more or less all patients with one of the three IBMF syndromes, Diamond-Blackfan Anemia (BDA), Fancona Anemia (FA) and Dyskeratosis Congenita (DA). This together with the optimal scientific environment allowed performing a number of unique clinical studies: long-term outcome of patients with an IBMF; correlation between genotype and phenotype of the different IBMFs; development of new tools for the diagnosis of DBA; clinical trials on the treatment of BDA evaluating new drugs.

For the acquired BMFs, the group concentrated on studies about clinical outcome of PNH (treatment with eculizumab; stem cell transplantation) as well as on research on residual hemolysis in PNH patients treated with eculizumab (pathophysiological mechanisms responsible for the residual hemolysis).

In both types of BMFs (IBMF and acquired BMF), the team has led to publications in high level journals such as in Blood, Am J Haematology, Haematologica. The published scientific work is highly original since only few groups in the world have access to data and biological material of such a high number of patients with these rare diseases. The scientific work has a relevant impact not only at the national but also at the international levels.

Assessment of the unit's academic reputation and appeal

Team 2 hosts the reference centre in France for the three mentioned IBMT as well as for acquired BMF, and particularly for PNH. This situation is the natural consequences of the team composition (opinion leaders in the field), the unique possibility to see patients from the whole country with these rare diseases and the possibility to collect data, as well as biological samples for on-going research. The reputation is not limited to France, but also extends at the international level. Scientists working on this team participate and conduct international clinical studies within the EBMT, the CIBMTR and other international societies.

For aplastic anemia and PNH, there is a long history of involvement within the Hospital of St. Louis. The department of Hematology is considered as the reference centre for both, SAA and PNH in France and is highly recognized internationally in Europe (EBMT) but also in the USA and Asia.

Team 2 has attracted students and residents internationally.

One of the members is an expert reviewer for DBA at the Orphanet (portal for rare diseases and orphan drugs).

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

The main social impact of team 2 is its strong interaction and active involvement within the specific patients' groups for the individual BMF syndromes. Here, the leaders organize structured teaching and information meeting for the patients and relatives, and have active interaction with the patients' organizations.

Team 2 staff is also involved in the "Aplastic Anemia & MDS International Foundation", which is the world's leading health organization dedicated to supporting patients and families living with aplastic anemia, MDS, PNH and related BMF diseases.

Assessment of the unit's organisation and life

Scientifically, the organization is clear, coherent and logical objectives in mind, which are the systematic clinical evaluation of BMF patients, and the research on pathophysiological mechanisms explaining the correlation between genotype and phenotypic presentation. The most important resources for their clinical and biological research are the patient databases as well as the biological material collected for studies. Both resources are easily accessible and can be utilized for research. The team staff has regular meetings discussing clinical aspects of the patients and results of their research. However, the two subgroups (IBMF and acquired BMF) do not have a standardized platform for planning and administrating their research and the common requisite for resources. Neither do they have a structured platform with the unit director.

Assessment of the unit's involvement in training through research

Members involved in team 2 are regularly training students, fellows and residents who have the unique opportunity to learn and to perform research on a high number of BMF patients. Furthermore, the permanent members give to the young researchers in training the opportunity to present studies at high levels national and international meetings, such as for instance ASH, EHA, EBMT annual meetings, and to be involved as first authors in publications.

Furthermore, the members involved in team 2 are actively involved in teaching of hematology at the local, national and international levels. They are participating in the elaboration of national and international guidelines.

Because of the small size of the group participating to Team 2, so far there is no structured training program for doctoral students and MD-PhDs.

Assessment of the five-year plan and strategy

The 5-year plan and the future strategy are based on the patient registries and the biological sample collections that have been constituted during the last years.

It is planned to concentrate on leukemogenesis and analysis of cell cycle performed on the biologic samples collected from FA patients. Extended genetic characterization for the other BMF syndromes are also planned: BDA patients sequencing of the RP gene is planned in order to better characterize phenotypic and genotypic correlations. In PNH patients, attention will be given to the screening for genetic mutations and polymorphisms that could explain incomplete response to eculizumab. New generation drugs for the treatment of patients with PNH will be evaluated as soon as possible.

For any type of BMF syndrome, clinical studies based on the different registries, as well as national and international collaborative projects will continue to be performed.

The 5 year strategy is original and credible, since everything is available (patient registry, patients' biological samples, infrastructure, know-how).

The strategy is consistent with what has been obtained so far.

Conclusions

- Strengths and opportunities:
  - The team gathers the key opinion leaders in IBMF and acquired BMF (aplastic anemia and PNH).
  - In IBMF, a nearly complete overview of the patients in France, a complete database, and a biologic sample collection are available.
  - The group hosts the Reference centre for IBMF and PNH in France and has an international reputation in the field.
  - The team 2 staff had published a high number of publications in journals with high scientific impact.
  - The team 2 staff has established good connections (support and networking) with genetic laboratories.
  - The registries that have been constituted as well as the systematic collection of biologic samples from patients with rare diseases, allow to continue research and maintain leadership in the field.
  - There is a good clinical support based on key opinion leaders in St-Louis and Robert Debré Hospitals.
  - The next generation researches in BMF could benefit from the infrastructure and know-how already available.
- Weaknesses and threats:
  - This is a relatively small group, based mainly on the two opinion leaders.
  - There is no structured program for doctoral students and MD-PhD training.
  - There is a lack of standardized platform for administrative issues.
  - There is a risk of losing the leadership and reputation because of lack of resources.
- Recommendations:

The team should organize a structured platform for administrative issues within Team 2 (IBMF and acquired BMF subgroups) and within the unit in order to optimize resources needed for on-going research.

The team should actively prepare a package for doctoral student and MD-PhD training and development of a public relation structure to attract students and fellows from France and abroad (rather within the unit than within the Team 2 alone).

Team 3 : HSCT

Name of team leader: Mr Régis Peffault DE LATOUR and Ms Eliane GLUCKMAN

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			
N3: Other permanent staff (without research duties)	4	4	4
N4: Other professors (PREM, ECC, etc.)	1	1	1
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	4	4	4
N6: Other contractual staff (without research duties)	4	4	4
TOTAL N1 to N6	13	13	13

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	0	
Theses defended	0	
Postdoctoral students having spent at least 12 months in the unit	0	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	2	2

Detailed assessments

Assessment of scientific quality and outputs

One of the two coordinators has pioneered the development of cord blood transplantation. He established the Eurocord data which is a world ressource leading to several important publications in the area. The scientific quality of the publications is particularly important, original with high impact factors in journals like Blood, Lancet Oncology, J Hepatol, J Clin Oncology... A significant number of publications are unique and world ressources in the field of hematopoietic stem cell transplantation.

Assessment of the unit's academic reputation and appeal

This team is cochaired by two coordinators and has two research axes. One coordinator has been recognised with various international awards and the other one has established an academic transplant program in association with the Hospital Saint Louis service with whom he closely works as well as with transplant issues with other colleagues in the unit.

The academic reputation is undisputable, particularly for cord blood transplantation, including numerous major contributions to international projects, numerous awards. The unit members involved in team 3 have worldwide broad international scientific connections.

Team 3 staff has been frequently appealed for educational programs in national or international meetings.

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

The main social impact is the strong interactions and active involvement in structured teaching and information meetings for the patients and their relatives, at the national and international levels (SFGM-TC, EBMT).

Assessment of the unit's organisation and life

The tasks are organized with a coherent and logical scientific objective in mind combined with a very important recruitment.

Assessment of the unit's involvement in training through research

Training through research is a constant goal of team 3 staff, recruiting residents or assistants from all over the country and abroad who are trained in clinical research, including data collection, statistical analysis, presentations in meetings and often first authors of articles in international peer reviewed journals, as well as obvious high level teaching through the European School of Haematology, which is headed by one co-coordinator.

Assessment of the five-year plan and strategy

The strategy and the assessment plan for the future remain at a high level but vulnerable for the Eurocord project. The long-term future of Eurocord remains elusive while lacking a senior clinician. Finally, the strategy could be highly valorized by crosstalking this clinical research with basic and translational researchs performed in an other unit on the same site .

Conclusions

- Strengths and opportunities:
  - The Saint-Louis transplant group has the more important recruitment in France and the registry is unique in the field.
  - This leadershisp has conducted to a production of a high number of publications in journals with high scientific impact.
  - The team has a an excellent clinical support.
  - It has also excellent connections with the GVHD translational lab.
- Weaknesses and threats:
  - The organization is coherent with logical scientific objective in mind combined with a very important recruitment.
  - However, there is no clear perspective concerning the long-term future plan for Eurocord leadership or stable funding. This is a unique network led by an international expert, still completely involved in the project, but who retired 7 years ago. The long-term prospect has not yet been solved and there is a big threat that the while organization of Eurocord and its scientific contribution could be displaced to another transplant center in France or abroad. This could represent a huge loss for the unit and for the Hospital St. Louis.
- Recommendations:
  - Clinical research shoud be integrated with the basic and translational research team, and performed on the same site by other members of the same clinical team.
  - The leadership for Eurocord should be maintained in the team and this may involve a in house long-term strategy otherwise the general stategy of Eurocord should be reconsidered in view of loss of leadership.

Team 4 : Adult primary immune deficiencies

Name of team leader: Mr Eric OKSENHENDLER

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	1	1	1
N2: Permanent EPST or EPIC researchers and similar positions			
N3: Other permanent staff (without research duties)	2	2	2
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	1
TOTAL N1 to N6	4	4	4

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	0	
Theses defended	0	
Postdoctoral students having spent at least 12 months in the unit	0	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	1	1

Detailed assessments

Assessment of scientific quality and outputs

The expertise is original and unique in France. It is based on the DEFI (Adult primary immune deficiencies) program launched in 2004. This program has included so far 738 patients which is a hudge cohort. A very well organized network has been set up in France headed by the team leader. All the clinical and biological data are centralized in St-Louis Hospital with a comprehensive clinically annotated biobank allowing prospective biological analyses. Phenotypic analysis is performed for each patient. Originally, screening of siblings has been established for more than one third of the patients. This database has led to publication of very important papers (more than 15 publications in high impact factor journals in Blood, J Clin Immunol, Transplation, Curr Opin HIV AIDS, AIDS...) describing the clinical and biological features of CVID during the last five years.

The coordinator has also described new entities such as patients having LOCID phenotype or CD19 deficiency. Based on kinetic studies, the team has underlined the advantages of SC IgG replacement as compared to IV substitution, which has an important clinical impact in daily practice. They also described the role of FcRn polymorphism in IgG replacement efficacy.

The research conducted has significantly contributed to a better understanding and diagnosis of immunodeficiency as well as to better treatment modalities.

Assessment of the unit's academic reputation and appeal

The coordinator has earned an undisputable international reputation in the field of primary immunodeficiencies and is recognized as a leader in France and worldwide. He collaborates within a European consortium on lung complications of CVID patients. He has developped collaborations with foreign groups in Europe and USA. He actively contributed to integrate the majority of French centers who recruited CIVD patients, even those with a low number of patients, participating in local centers in France by giving talks and conferences. The coordinator involvement in international networks has been developped during the last years and should be reinforced in the future (ie STILPAD). Students supervised by the team 4 coordinator have been involved in publications and MD thesis.

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

The team 4 coordinator participates to annual meetings of national patient groups.

Assessment of the unit's organisation and life

This team involves a group which has a critical size and has to attract collaborators. However, the scientific program is coherent and the biobank ressources can be considered as a major source of potential biological studies. The organisation of the DEFI program could potentially integrate young physicians to coordinate clinico-biological studies. Updating of the database is currently performed by a dedicated half-time working person, with the aim of having a full time dedicated person.

Assessment of the unit's involvement in training through research

Two publications have been performed by medical doctors under the team 4 coordinator supervision. The group hosted a medical doctor coming from Canada for 6 months.

Assessment of the five-year plan and strategy

Future aims are ambitious but feasible based on what has been previously achieved. Projects related to team 4 aim to develop clinical and biological studies on CVID and to describe new entities. To achieve these aims it will be necessary to reinforce human ressources in the field of data management, of clinical research.

Conclusions

- Strengths and opportunities:
  - The coordinator has a unique clinico-biological database on combined variable immune deficiencies.
  - This unique leadership resulted in a very good level of publications.
  - The strategy raises the possibility to assess long-term follow-up of patients and to describe specific and poorly known late-onset complications.
  - The group is involved in important international collaborative projects.
  - The coordinator is considered as an international key opinion leader.
- Weaknesses and threats:
  - The group has limited human ressources and the team 4 coordinator has to assume most organisational, management and teaching tasks on his own.
  - The collaborative basic research is still limited.
- Recommendations:

It is important that this team takes advantage of the translational platform available in St-Louis hospital and of attracting young physicians and students to reinforce the manpower dedicated to research projects. The coordinator has to increase industrial fundings and collaborations and to develop basic and translational research projects with co-supervision of Masters or PhD students.

5 • Conduct of the visit

Visit dates:

Start: Thursday 10 january 2013 at 15:00

End: Friday 11 january 2013 at 16:00

Visit site: Hôpital Saint-Louis

Institution: IUH, Paris 7 Diderot

Address: Rue Claude Vellefaux, Paris

Conduct or programme of visit:

Day one – 10 January 2013	
15:00	Welcome
15:05	AERES representative: the role and procedures of AERES
15:10	Presentation of the unit by the director
16:10	Team 1 - Acute leukemias
	Team leaders: Mr Hervé DOMBERT and Mr André BARUCHEL
17:10	Coffee break
17:15	Team 2 - Aplastic anemia and hereditary blood disorders
	Team leader: Mr Thierry LEBLANC
18:15	Parallel meetings with personnel:
	Discussions with engineers, technicians, administrative
	Discussions with staff scientists
	Discussions with students and post-docs
19:15-19h45	Debriefing on the team presentations

Day two – 11 January 2013	
9:00	Team 3 - HSCT
	Team leaders: Mr Régis Peffault DE LATOUR and Ms Eliane GLUCKMAN
10:00	Team 4 - Adult primary immune deficiencies
	Team leader: Mr Eric OKSENHENDLER
11:00	Coffee break
11:15-11:45	Discussion with the representatives of the managing bodies
11:45-12:15	Discussion with the head of the unit
12:15-13:30	Lunch
13:30-16:00	Private meeting of the visiting committee
16:00	End of the visit

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

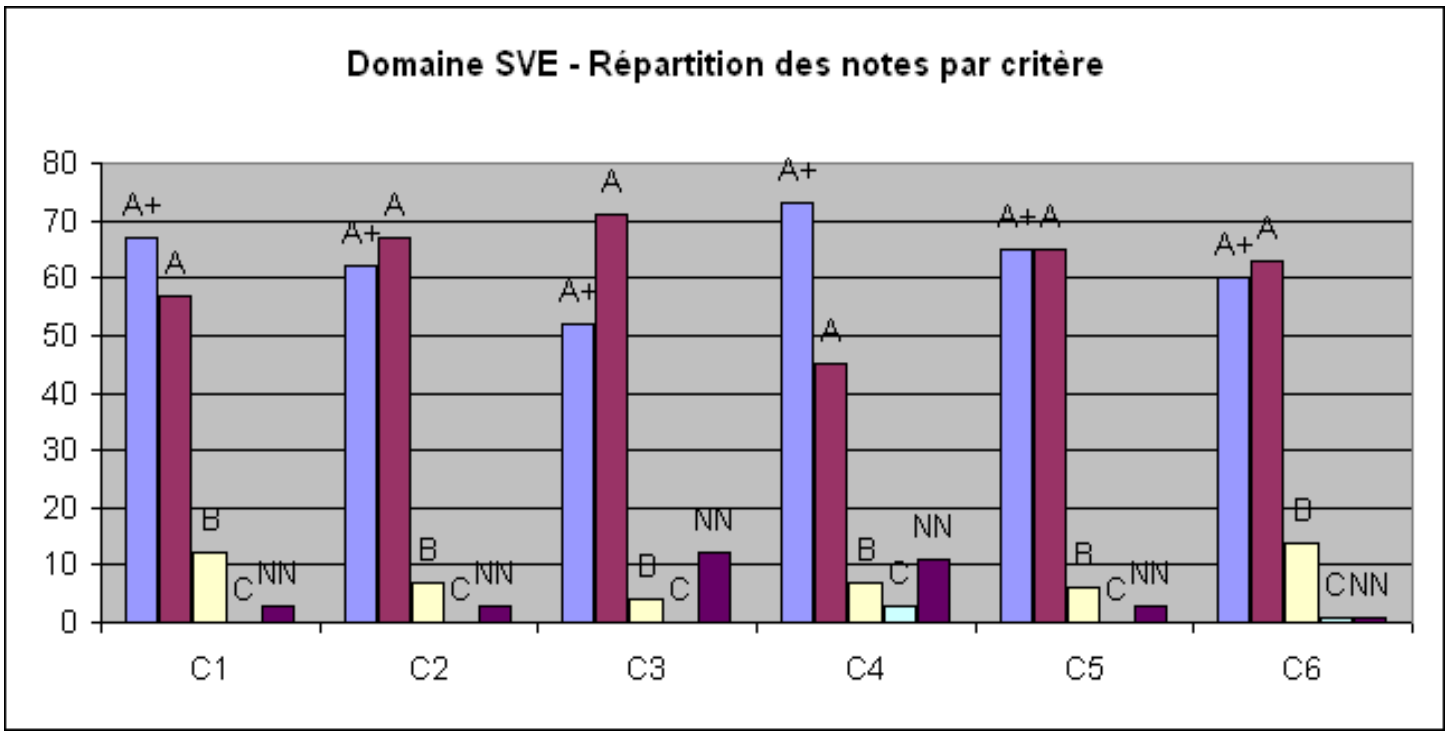
Grades

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

Le Président

P/VB/LB/NC/YM – 2013 - 123
Paris, le 29 avril 2013

M. Pierre Glaudes
Directeur de la section des unités de l'AERES
20 rue Vivienne
75002 PARIS

S2PUR140006343 - RECHERCHE CLINIQUE APPLIQUEE A L'HEMATOLOGIE - 0751723R

Monsieur le Directeur,

Je remercie les membres du comité de visite de l'AERES pour la production du rapport sur la situation du laboratoire « Clinical research in hematology, immunology and transplantation » et les remarques constructives formulées. Le directeur a élaboré dans sa réponse les éléments permettant de répondre aux recommandations du comité.

Je me réjouis des appréciations élogieuses qui sont portées sur ce laboratoire dont vous avez souligné l'excellent niveau qualitatif et quantitatif des publications et la position de leader de cette unité dans le domaine de la transplantation des cellules souches hématopoïétiques et des déficiences immunitaires primaires chez l'adulte.

Je note également que la stratégie de collaboration développée entre l'Hôpital St Louis, l'IUH et l'Université Paris Diderot est relevée, à juste titre, comme une force par le comité.

Je vous prie d'agréer, Monsieur le Directeur, l'expression de toute ma considération.

Vincent Berger

université PARIS DIDEROT PARIS 7

Tél +33 (0) 1 57 27 55 10
Fax +33 (0) 1 57 27 55 11
secretariat.president@univ-paris-diderot.fr
www.univ-paris-diderot.fr

Adresse Postale
Présidence
Grands Moulins
75205 Paris Cedex 13

SORBONNE PARIS CITE
RECHERCHE ENSEIGNEMENT SUPERIEUR

Institut Universitaire d'Hématologie (IUH) – Université Paris Diderot
EA3518, Recherche Clinique en Hématologie, Immunologie et Transplantation
Paris Alliance of Cancer Research Institutes (PACRI)
Hôpital Saint-Louis (AP-HP), Paris

18/04/13

Sujet:

Prof. Hervé Dombret, PU-PH

Directeur de l'EA3518
Recheche Clinique en Hématologie, Immunologie et Transplantation

Chef du Pôle Hématologie-Oncologie-Radiothérapie-Immunologie Clinique

Chef du Service des Maladies du Sand (Unité Leucémies)

La visite d'évaluation AERES de l'EA3518, qui s'est déroulée les 10 et 11 Janvier 2013, a permis de faire le point sur les activités et la production scientifique de l'unité, sur ce qui a été accompli depuis la dernière évaluation de Février 2008, et sur les orientations futures.

Tous les membres de l'EA3518 remercient profondément les personnes qui ont organisé cette visite et les membres du comité d'évaluation pour la qualité de leur écoute et la pertinence de leur rapport d'évaluation. Le comité d'évaluation a bien perçu le caractère « unique » et original de cette structure et les buts poursuivis par ses animateurs. Cette originalité s'accompagne bien évidemment de faiblesses et de menaces, qui ont été relevées, mais aussi de grandes forces et opportunités, qui ont été notées par le comité.

Quelques informations complémentaires peuvent être apportées :

1) En accord avec la Direction du Groupe Hospitalier, une réflexion a été engagée pour doter à très court terme le Pôle Clinique d'une « Unité Fonctionnelle (UF) de Recherche Clinique ». Cette UF devrait permettre d'abriter et d'afficher les activités de recherche clinique au sein des structures hospitalières, et d'y recruter ou rattacher des personnels médicaux ou non-médicaux (infirmières, techniciens). Il est prévu qu'Eurocord (composante de l'équipe 3) intègre cette UF, permettant ainsi au Pôle d'assurer le(s) recrutement(s) nécessaire(s) à sa pérennité sur le site.
2) Il a été désormais bien établi que les activités de recherche clinique dans le domaine des syndromes myélodysplasiques intégreront l'EA3518, dès l'arrivée de Pierre Fenaux sur le site en septembre 2013. Le Dr. Lionel Ades dirigera cette nouvelle composante de l'EA, soit sous la forme du 5ème équipe, soit au sein de l'équipe 1.

Hervé Dombret
Directeur de l'EA3518

HOPITAL SAINT-LOUIS
1 avenue Claude Vellefaux
Paris, 75475 Cedex 10

TELEPHONE
+33 (0)1 42 49 96 43

FAX
+33 (0)1 42 49 40 10

EMAIL
herve.dombret@sls.aphp.fr