EpiDermE - Epidémiologie en dermatologie et évaluation des thérapeutiques: du phénotype à la thérapeutique

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on research units and interdisciplinary research units

Epidemiology in dermatology and evaluation of therapeutics

EpiDermE

Under the supervision of the following institutions and research bodies:

Université Paris Est Créteil Val de Marne - UPEC

January 2014

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

Department for the evaluation of research units

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

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

On behalf of the expert committee,

- Ms Juliette MAZEREEUW-HAUTIER, chair of the committee

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

Evaluation report

This report is the result of the evaluation by the experts committee,the composition of which is specified below.

The assessment contained herein are the expression of independent and collegial deliberation of the committee.

Unit name:	Epidemiology in dermatology and evaluation of therapeutics
Unit acronym:	EpiDermE
Label requested:	EA
Present no.:	
Name of Director (2013-2014):	Mr Pierre WOLKENSTEIN
Name of Project Leader (2015-2019):	Mr Pierre WOLKENSTEIN

Expert committee members

Chair: Ms Juliette MAZEREEUW-HAUTIER, Toulouse University

Experts: Mr Sélim ARACTINGI, Paris Descartes University (representative of CNU)

Mr Paul LANDAIS, Montpellier 1 University

Mr Vincent LÉVY, Paris 13 University

Scientific delegate representing the AERES:

Mr Jean GIRARD

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

Mr Jorge BOCZKOWSKI, Paris 12 University

Mr José COHEN (Doctoral School of Paris 12 University)

Mr Georges GELLAEN, IMRB, Institut Mondor de recherche biomédicale

1 • Introduction

History and geographical location of the unit

EpiDermE (Epidemiolgy in Dermatology and evaluation of therapeutics) is a new unit to be created.

Historically, The Department of Dermatology was created during the late 60s. It constitutes with the Department of Plastic Surgery, The Federation of Dermatology and Skin Sciences. The Department of Dermatology is part of the Academic Department for Virus Immunity Cancers (VIC-DHU). The Department of Dermatology works in close collaboration with the Henri Mondor Clinical Investigation Centre (CIC). In 2008, the team of Dermatology participated in the successful creation of the "Laboratoire d'investigation clinique" EA4393.

The unit to be created will be located at the Faculté de Médecine, Créteil-Val de Marne, France.

The Department hosts 2 National Reference Centers (Neurofibromatosis and Auto-immune bullous diseases/severe cutaneous adverse drug reactions). The team developed specific research, mainly on these groups of diseases, either studying phenotype/genotype correlations, performing therapeutic trials or observational studies focused on toxic reactions to drugs.

The project includes two work packages, based on these 2 different approaches: WP-1: phenotype evaluation and WP-2 therapeutic evaluation.

Management team

The director of the unit will be Mr Pierre WOLKENSTEIN.

The work package 1 will be coordinated by Mr Pierre WOLKENSTEIN; the work package 2 will be coordinated by Mr Olivier CHOSIDOW. The coordinator for the methodological aspects will be Ms Laurence FARADET.

The management of each projects will be discussed by the team during meetings (weekly lab meeting, monthly data lab meeting, annual daylong meeting).

AERES nomenclature

SVE1_LS7

Unit workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	6 (1.7 FTE)	7 (2.0 FTE)
N2: Permanent EPST or EPIC researchers and similar positions		
N3: Other permanent staff (without research duties)	3 (0.9 FTE)	3 (0.9 FTE)
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	9 (2.6 FTE)	10 (2.9 FTE)

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken	4	
Qualified research supervisors (with an HDR) or similar positions	4	5

2 • Overall assessment of the interdisciplinary unit

The overall assessment of this unit creation is very favorable.

The aims of this project are as follows: 1-To create a research team devoted to clinical epidemiology (evaluation of phenotypes, therapeutics and their side-effects). 2- To offer teaching and research programs for master degree and PhD students. 3- To obtain funding from Academic sources or 4- Private sources.

Strengths and opportunities related to the context

The expert committee noted that the group had the following strengths:

- An already established international reputation and high level publications in the international literature;

- Well annotated cohorts of rare diseases (hidradenitis suppurativa, neurofibromatosis, severe cutaneous adverse reactions to drugs);

- Diversified collaborations with different basic research teams (especially with Immunology and Genetic teams) that allows them to be part of successful translational projects;

- Dynamic team composed of various and complementary profiles (mainly Dermatologists but also internal medicine, Rhumatologist, Pharmacist);

- Strong support from the University;

- Strong ability to find fundings.

In conclusion, the group has all the techniques and competence to lead this project (background, publications, financial support and adequate scientific collaborations).

Weaknesses and threats related to the context

The expert committee, however, noted the following weaknesses:

- Five-year plan: It is more a continuation of previous research than a real novel innovating project. However, the oral presentation and an updated project highlighted the lines of force of the project, the presentation of which was not extended in the initial document;

- Too many axes of research related to several diseases to be studied without links between each other;

- Insufficient involvement in training since to date only one PhD student was trained by the team.

Recommendations

The expert committee recommends the following:

- The team needs to focus on the strongest topics (neurofibromatosis, scabies and lices, severe drud-induced side-effects);

- The team should make efforts to recruit full time PhD students, not only clinicians, but also students with a science curriculum.

3 • Detailed assessments

Assessment of scientific quality and outputs

The team has developed specific research based on the evaluation of phenotype/genotype correlations of diseases such as neurofibromatosis type I, hidrosadenitis suppurativa or severe drug reactions. Such research has required a first step of constitution of large cohorts, specialized clinical evaluations of patients and biological banking. Further steps have required closed collaboration with other teams (i.e. genetic laboratory for molecular analysis of neurofibromatosis type I).

The main results are as follows:

- For neurofibromatosis: identification of a phenotype associated with malignant nerve tumors and identification of a modifying gene (ANRIL);

- For hidrosadenitis suppurativa and severe drug reactions: clinical descriptions of cohorts;

- The team has also developed therapeutic trials: oral ivermectin vs. malathion for head lice and open trial on cyclosporine for severe drug reactions.

The originality of this research is notable.

Some results had a direct impact on patient's clinical care (i.e. results on head lice's therapy with ivermectin or identification of phenotype associated with malignant nerve tumors in neurofibromatosis type I).

The team reported many publications. There are 93 original papers cited in the original document, including 41 on the main topics (neurofibromatosis: 22, drug reactions: 10, hidrosadenitis: 5 and head lice : 4). Five other papers were published since the initial document (neurofibromatosis : 4, head lice: 1).These papers were published in the best quoted Dermatological journals but also in prestigious international generalist journals (i.e. N Engl J Med, J Natl Cancer Inst).

Assessment of the unit's academic reputation and appeal

Mr Pierre WOLKENSTEIN and Mr Olivier CHOSIDOW are internationally recognized leaders in the topics of neurofibromatosis and head lices, respectively (i.e. editorials on the topic, communications or lectures at national or international meetings).

Mr Olivier CHOSIDOW is the director of French satellite Skin Cochrane and Vice-president of the non-cancer national PHRC committee.

There are 2 national reference centers for rare diseases in the Department (Neurofibromatosis and Auto-immune bullous diseases/severe cutaneous adverse drug reactions).

The team coordinates National and European networks (i.e. NF France, Regiscar, and member of scientific committee of the Rare Disease Cohorts (RADICO) program (PW).

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

The team interacts with patients' associations (i.e. Neurofibromatose de type 1, Conseils et aide aux patients victimes du syndrome de Lyell.

The unit also has a project of building e-cohorts of patients.

The team has several contracts with industry (i.e. Novartis), with the ANSM (National Agency of Drug Safety).

Radio Interviews (i.e. France Culture).

Assessment of the unit's organisation and life

The unit’s organization is coherent and convenient for unit strategy and interdisciplinary approaches.

Assessment of the unit's involvement in training through research

Only one doctorant (MD) was trained to date by the team, but the new team’s organization seems appropriate for attracting and coordinating future students' training, especially for young clinicians with a special interest in Dermatology.

Assessment of the strategy and the five-year plan

The overall project can be considered as a continuation of previous research projects.

The project is based on the recognized expertise of the team, especially in terms of methodology in therapeutics trials, cohort’s constitution and phenotype analysis.

For neurofibromatosis, the objective is to develop a novel classification of patients. This classification will be useful for further work on modifying genes. The perspective is to identify new therapic targets for patients’ therapy. The team is also considering targeted therapeutic trials with novel agents (anti MEK).

For hidrosadenitis suppurativa, the team is working on the elaboration of a e-cohort of patients with the aim of forming a large representative cohort in order to analyze the natural history of the disease.

For severe drug reactions: the team is planning a therapeutic trial comparing topical steroids to systemic steroids for DRESS syndrome (“drug reaction with eosinophilia and systemic symptoms). Another objective is to analyze the database in order to identify prognosis factors. For skin rashes, the objective is to find correlations between phenotype and etiology (virus or drug).

For scabies, a therapeutic trial comparing ivermectine to topical permethrine will be performed.

The overall project is satisfactory in terms of credibility, feasibility and risk-taking. The topics are not highly competitive.

In conclusion, in the past the team proved its capacity to perform original and high level research in the field of phenotype evaluation and therapeutics in the domain of skin diseases. The project of the unit EpiDermE is well constructed and therefore promising. It should therefore be supported.

4 • Conduct of the visit

Visit date:

Start:	January 31, 2014
End:	January 31, 2014

Visit site	Faculté de médecine de Créteil
Institution:	Faculté de médecine de Créteil
Address:	8, rue du Gal Sarrail, 94000 Créteil, France

Conduct or programme of visit:

10h00 - 10h30 :	Réunion à huis-clos du comité de visite
10h30 - 11h00 :	Contexte et présentation générale : M. Pierre WOLKENSTEIN
11h00 - 11h15 :	Discussion
11h15 - 13h15 :	Projet scientifique
	- Work package 1 : Evaluation des phénotypes
	- Work package 2 : Evaluation des thérapeutiques
13h15-14h15 :	Repas
14h15 - 14h45 :	Réunion avec les tutelles
14h45 - 15h15 :	Rencontre avec les chercheurs sans le porteur de projet
	Rencontre avec les futurs étudiants, doctorants, postdoctorants
15h15 - 16h00 :	Délibération à huis-clos / comité d'experts
16:00	Départ des participants

5 • Supervising bodies' general comments

UPEC
Connaissance - Action

UNIVERSITÉ
PARIS-EST CRÉTEIL
VAL DE MARNE

Réponse au rapport du comité d'experts AERES suite à l'évaluation
Epidemiology in dermatology and evaluation of therapeutics

Titre de l'unité : EpiDermE
Label demandé : EA
Nom du Directeur : Pr. Pierre Wolkenstein

We first would like to thank the review committee for its strong support to our project. The committee considered that the research topics addressed by our group are relevant, that we have already an important scientific production and an international reputation. It highlighted that our main strengths are well annotated cohorts of rare diseases, collaborations with different basic research teams for successful translational projects, multidisciplinarity and the ability to find funding.

This positive evaluation will facilitate setting up a policy to foster the recruitment of a permanent scientist and/or technician and also the attractiveness for students.

The review committee made a few remarks and our responses are detailed herein:

Concerning the five-year plan, we apologize for the misunderstanding and want to clearly claim that for the period 2015-2019 we will focus on our lines of force ie neurofibromatosis, hidradenitis suppurativa, scabies and lice, severe adverse drug reactions . It is only when our major objectives will be reached that we will enlarge the activities of the submitted project.

Concerning the involvement in training we planned to increase the number of PhD students to at least 4. Indeed our team will be attractive to clinicians but also to scientists as it will be the only one in France on the topic of epidemiology in dermatology. The team will be also able to generate grants for students toward industry such as pharmaceutical firms (bourses CIFRE) but also cosmetics.

In the concluding remarks it was stated 'The overall project is satisfactory in terms of credibility, feasibility and risk-taking. The topics are not highly competitive'. We considered that scabies and lice, cutaneous side effects of drugs are highly competitive topics due to their important impact in terms of public health.

The team and the University would like to thank again the committee for its support and advice. We hope that the members of the committee will follow our work with satisfaction.

Sincerely yours,

Pr Pierre Wolkenstein
Head of the research group EpiDermE

Luc Hittinger
President of UPEC