



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

Section des Unités de recherche

## Report from the visiting committee

Research unit : Infection à mycobactéries

(tuberculose, lèpre, mycobactériose) et antibiotiques :  
aspects moléculaires, thérapeutiques et

épidémiologiques – EA 1541

University Paris 6

February 2008



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## Rapport du comité d'experts

Unité de recherche : Infection à  
mycobactéries (tuberculose, lèpre,  
mycobactériose) et antibiotiques :  
aspects moléculaires, thérapeutiques et  
épidémiologiques

de l'Université Paris 6



Section des unités  
de recherche

*Le Directeur*

**Jean-Jacques Aubert**

February 2008



# Report from the visiting committee

## The research unit :

Name of the research unit : Infection à mycobactéries (tuberculose, lèpre, mycobactériose)  
et antibiotiques : aspects moléculaires, thérapeutiques et épidémiologiques

Requested label : EA

N° in case of renewal : 1541

Head of the research unit : Mr Vincent JARLIER

## University or school :

University Paris 6

## Other institutions and research organization:

## Date(s) of the visit :

14-15 February 2008



# Members of the visiting committee

## Chairman of the committee :

Mr Jean-Laurent Casanova, Paris

## Other committee members :

Mrs Andrea Cooper, Trudeau Institute, USA

Mr Charles Bangham, UK

Mr Frédéric Geissman, Paris

Mr Jean Dubuisson, Lille

Mr Guido Poli, Milano, Italy

Mr Joost Van Meerwijk, Toulouse

Mrs Pascale Mercier, Toulouse

Mr Camille Locht, Lille

## CNU, CoNRS, CSS INSERM, représentant INRA, INRIA, IRD.....) representatives :

Mr Michel Drancourt, Marseille, CNU representative

# Observers

## AERES scientific representative :

M. Nicolas Glaichenhaus

## University or school representative :

Mrs Jacqueline Capeau, University Paris 6

# Report from the visiting committee



## 1 • Short presentation of the research unit

- Number of lab members with teaching duties : 4 including 1 PU-PH and 3 MCU-PH
- Number of engineers, technicians and administrative assistants : 4
- Numbers of HDR : 1 + 2 pending
- Numbers of PhD. Students who have obtained their PhD since : 13
- Average length of a PhD during the past 4 years : 4 years
- Numbers of PhD students currently present in the research unit : 4
- Number of PhD students with fellowships :
- Number of « publishing » lab members : 4 out of 4

## 2 • Preparation and execution of the visit

The visit started by a 15 minutes presentation by the director the Unit. This was followed by 30 minutes presentation by each of the 4 team leaders.

## 3 • Overall appreciation of the activity of the research unit, of its links with local, national and international partners

The head of this unit is a senior researcher with both clinical and teaching duties (PU-PH). Research topics include (1), the molecular targets of anti-mycobacterial agents, (2) the mechanisms of acquired resistance to anti-mycobacterial agents, (3) experimental chemotherapy and (4) epidemiology of resistance to anti-mycobacterial agents.

The research is overall well focused on the various aspects of anti-mycobacterial therapeutic strategies, covering different aspects on the same theme. The different teams have obvious complementary expertise. The research unit as a whole has a well-recognized expertise in anti-mycobacterial drug testing. This expertise has been acquired over many years, and several generations of excellent unit leaders.

In addition, the National Reference Center for mycobacteria is hosted by the unit. This shows that the unit is well connected nation-wide. The National Reference Center adds a very important richness to the unit, as it gives access to different strains, with different resistance characteristics. It also allows the research unit to be informed at first hand on the evolution and epidemiology of anti-bacterial resistance in France. This is the main subject of one of the teams.

There is a very good integration of basic research and clinical/industrial research. The unit benefits from several contracts with industry. They have been very actively involved in the testing of diarylquinoline, one of the few new drugs currently being developed. This drug is one of the most promising break-through in the field of anti-mycobacterial therapy. This work has been published in Science in 2005, with the Head of the Unit as the last author.



Despite close contacts to industrial partners, there is, however, little technological innovation, and no patents have been applied for in recent years.

The publication record of the entire unit is good, with roughly 40 articles published in international journals over the last 5 years. Most of these articles are published in relatively good journals of the discipline (Clinical Microbiology and Antimicrobial Agents), up to the level of the J. Clin. Microbiol. and Antimicrob. Agents Chemother. Very few (with the exception of an article in Science) were published in multidisciplinary journals of high impact.

The head of the unit has been invited to deliver lectures in several French and European meetings. However, this is much less the case for the other team leaders. The involvement of the research unit in the large international and European initiatives is rather modest (e.g. no involvement in FP6, FP7 programmes).

#### 4 • Specific appreciation team by team and/or project by project

- **Team 1 : Epidemiology of mycobacterial infections and their resistance to antimicrobials**

The head of this team is a junior researcher with clinical and teaching duties (MCU-PH). Axis of research include epidemiological studies and the study of the impact of new strategies of management. Reasonable and solid research, that however would benefit from more ambitious scientific goals.

- **Team 2 : Experimental chemotherapy of mycobacterial infection**

The head of this team is a junior researcher with clinical and teaching duties (MCU-PH). This team has a very practical and useful goal: to develop new chemotherapeutic regimens for treatment of mycobacterial infection. There is sufficient expertise in the team and they cover the development of chemotherapeutic regimens not only for TB but also other mycobacterial diseases such as leprosy and Buruli ulcer. This is highly commendable. The team publishes in respectable peer-reviewed journals. The principal concern was that the team leader did not have a strong apparent commitment to developing mechanistic insight into the models in question. While the practical aspects of the work will have (and indeed have had) high clinical impact, without mechanistic insight the scientific impact of the teams work will be limited. The professional development of the team leader should be a focus of the Unit Head.

- **Team 3 : Molecular targets and resistance mechanisms of anti-mycobacterial drugs**

The head of this team is a junior researcher with clinical and teaching duties (MCU-PH). The research carried out by this team is very complementary to that of the other teams. It involves several basic aspects and potential novel approaches, combining molecular biology with structural biology. The research activity is essentially a continuation of previous research by the team. It is focused on topoisomerases, inteins and ATP synthase, the latter of which is a follow up of the highly successful work on diarylquinoline. However, given the size of the team, it is not clear whether it will be competitive in all these activities. The publication record of the team leader over the last five years is modest to correct, with so far still few invited lectures and international activities. However, the team leader has spent a post-doctoral year at the University of London (2005), which has resulted in two publications. It is hoped that in the next few years the team leader will emerge as a real leading figure in the field. This would be facilitated by the group's participation in new, important international programmes on tuberculosis and anti-mycobacterial compounds.

#### 5 • Appreciation of resources and of the life of the research unit

- **Management :**

The management of the research unit is excellent. The head of the unit is obviously very energetic and charismatic. The unit is well organized, and the different teams are complementary. The research covers a continuum from epidemiology of anti-mycobacterial drug resistance, in particular in France, over applied research in drug testing, both in vitro and in vivo, to basic understanding of drug resistance and mode of action. This includes molecular approaches and structural biology.



- **Human resources :**

Human resources are adequate. There is a good balance between senior scientists, technical staff and students. All senior lab members actively participate in research and publish in international journals. The overall length of a PhD is an acceptable 4 years, and with 3 “HDR” (one already obtained + 2 pending), training of the students should be satisfactory.

It may, however, be useful to recruit a full-time scientist, and also to recruit post-doctoral fellows. This would certainly speed up, essentially the basic research activities, to make them more competitive.

- **Communication strategy :**

The communication was very good. The document was clear, and the presentations were dynamic, well structured and balanced.

## 6 • Recommendations and advice

- **Strengths :**

A broad range of approaches that are well integrated and focused on the research of anti-mycobacterial drugs. The lab benefits well from being the French National Reference Center for mycobacteria. It also benefits well from its collaboration with Pharmaceutical companies. There is great enthusiasm and seriousness. The research is goal- and drug-oriented yet also interested in deciphering the mechanisms of action of anti-mycobacterial drugs. There is high productivity, especially given that this is a clinical and university laboratory without any institutional support from the main related French research governmental agencies (CNRS, INSERM, ANR). In this context, the laboratory intelligently addresses questions that they can solve. Their Science paper is a landmark paper, perhaps the discovery in the treatment of tuberculosis in the last five or ten years.

- **Weaknesses :**

It is not clear if and how the three junior researchers (MCU-PH) intend to progressively develop a more independent line of research in the future. It is surprising not to see a list of patents, given the theme of the lab and their connection with pharmaceutical companies. There is also an insufficient interest in attempting to decipher the ‘global picture’ of tuberculosis: there are not enough international collaborations, even with human and mouse immunologists, but also with clinicians and human (as opposed to microbial) epidemiologists.

- **Recommendations :**

The laboratory is encouraged to continue the good work along the established lines of research and with the current strategy and organization. A support from French research governmental agencies would be helpful to boost the laboratory’s research. Junior members should be encouraged to seek international recognition. The participation in large international programmes, such as FP7, and Grand Challenge programmes, should be encouraged. More generally, international collaborations should be strongly encouraged, in particular with scientists interested in other aspects of tuberculosis (immunology, human genetics, etc.).

**Conclusion** : top 25% internationally in its field