Laboratoire de microbiologie, adaptation et pathogénie

Rapport Hcéres

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

Section des Unités de recherche

AERES report on the research unit

Microbiologie Adaptation& Pathogénie

From the

Université Lyon 1

INSA de Lyon

CNRS

Mai 2010

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et de l'enseignement supérieur

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Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

Mai 2010

Unit

Name of the unit: Microbiologie Adaptation& Pathogénie

Requested label: UMR CNRS

No. in case of renewal: UMR 5240

Unit director: Ms. Nicole Cotte-Pattat

Members of the expert committee

Chairperson:

M. Didier Mazel, Institut Pasteur, Paris

Reviewers:

M. Pierre Abad, Université de Nice-Sophia Antipolis

Ms. Carmen Buchrieser, Institut Pasteur, Paris

Mr. Jean-Marc Ghigo, Institut Pasteur, Paris

Ms. Alexandra Gruss, INRA, Jouy-en-Josas

Mr. Michael Steinert, Institut für Mikrobiologie, Braunschweig, Allemagne

Reviewer(s) nominated by the staff evaluation committees (CNU, CoNRS, CSS INSERM ...):

Mr. Jean Pierre Rousset, CoNRS member

Representatives present during the visit

Scientific delegate representing AERES:

Ms. Claire Poyart

University representative :

Mr. Jean-François MORNEX, University Lyon 1

Mr. Jean-Marie Reynouard, INSA

Research organisation representative :

Mr. Bertrand Daignan-Fornier, CNRS representative

Report

1 • Introduction

- Date and conduct of the visit:

The expert committee visited the Laboratory on February 11 2010. The meeting started with a presentation by the current head of the laboratory. Subsequently, each team presented its past activities and future projects. Experts also met, in separate committees, with representatives of: researchers with permanent positions, PhD students, postdoctoral fellows, engineers, and technicians and administrative assistants. The committee also met with representatives of the University, INSA, Bayer CropScience, and the CNRS. A final meeting was held with the director. The site visit ended with the closed-door meeting of the committee.

- History and geographical location of the unit and brief description of its field of study and activities:

The laboratory is located in the A. Lwoff building on the University Lyon I campus (Domaine de la Doua). This research unit "Microbiology Adapatation & Pathogeny »" UMR CNRS 5240 has been under the directorship of Ms. Nicole Cotte-Pattat for the past 5 years, and consisted of 6 teams This Unit resulted from the fusion in 2005 of the UMR5122 and UMR2847. In 2008, the people of team 6 that were still on the Lyon I campus moved to the site "de la Dargoire" to merge with the other members already present in the lab hosted by their Industrial partner BayerCropScience. The scientific scopes of the research in the UMR deal with environmental microbiology, focusing on two major bacterial species, Erwinia chrysanthemi and Legionella, phytopathogen fungi and yeast. This research is based on approaches that include molecular genetics, biochemistry, genomics and bioinformatics. The studied microorganisms are often model organisms of major interest for fundamental research as well as for applications in biotechnology, the food industry and the medical sciences.

- Management Team:

Nicole Cotte-Pattat and D. Job/C Bruel, as a past/future Deputy Director, direct the Research Unit. A Team council consisting of the individual team leaders meet with the Director and Deputy Director twice a month.

- Staff members (on the basis of the application submitted to the AERES:

	In the report	In the project
N1: Number of professors (see Form 2.1 of the unit's dossier)	19	18
N2: Number of EPST, (Public scientific and technological institution) or EPIC, (Public industrial and commercial institution) researchers (see Form 2.3 of the unit's dossier)	11	10
N3: Number of other professors and researchers (see Form 2.2 and 2.4 of the unit's dossier)	11	6
N4: Number of engineers, technicians and tenured administrative staff members (see Form 2.5 of the unit's dossier)	14,9 ETP	15,9 ETP
N5: Number of engineers, technicians and non-tenured administrative staff members (see Form 2.6 of the unit's dossier)	5	0
N6: Number of doctoral students (see Form 2.8 of the unit's report dossier and 2.7 of the unit's project dossier)	13	22
N7: Number of persons accredited to supervise research and similar	26	23

2 • Assessment of the unit

- Overall opinion:

Globally, the research carried out at the Unit can be qualified as good. The Unit is clearly visible in the French and international research landscape. However, the committee noticed heterogeneity in the performances of the various teams, such that the quality and originality of the research of some teams were clearly at high international standard, while others were less performant. This is also evident when one considers the level of funding that the various teams can attract into the Unit. However on the whole, the unit groups have been very successful in grant applications – they increased external funding by 4-fold during the last 4 years. The director and the staff scientists of the unit proposed a new project for the next term with several adjustments, taking into account the recent developments in the different former teams. This is the case for instance in the choice to close the project of former team 3, due to a recurrent problem of funding, and concomitant creation of a new team (2) from part of former team 1 and team 3, coupled with a move toward new approaches, or the changes made in the management board for team 6.

- Strengths and opportunities:

This Unit provides a prime example of the value of an association CNRS & University by providing excellence in teaching, research and the training of PhD students. They trained more than 50 master 2 students and 24 PhD during the last period and produced more than 130 publications in journals with good to high visibility. The different teams

have been able to tie excellent collaborations, national and international, giving them access to cutting-edge technologies and/or knowledge. The team gathering all the research on phytopathogen fungi is hosted by Bayer CropScience, and the results of this day-to-day association is undoubtedly positive, not only in terms of knowledge transfer and applications, but also in terms of research quality as attested by the level of external funding and publication records.

- Weaknesses and threats:

The major threat stays in the dispersion, both scientific and geographical. The Unit gathers 6 teams located in 2 distant places, and working on different bacteria (though mostly on E. chrysanthemi and more recently Legionella), on yeast and on two phytopathogen fungi. The committee did note that there had been a real effort of reorganization in the project presented, with the abandon of certain projects and re-focusing on certain others; nevertheless, the risk of non-competitiveness in a few projects is real, especially with the start of some new projects from little preliminary evidence and involving only a limited number of researchers in highly competitive fields. Some teams are not attracting external funding, nor post-docs or PhD students. One general problem for several teams results from the heavy teaching load of their members.

- Recommendations for the unit director:

The management of the unit should maintain its effort to guarantee the cohesion of the unit by insuring regular meetings involving the scientists of the two geographical sites. This would be particularly important for the fungi team, where the Unit director should carefully accompany the progressive disengagement of the former leader (until 2012), to help them to maintain their excellent scientific production during the transition.

The new director is facing another important challenge with the development of small teams of which some work on a large spectrum of unrelated projects and that have weak scientific productivity (though partly due to heavy teaching loads). A support to such dispersion is unlikely to be the best solution for the science, and in term of institutional politics may lead to long-term problems. The committee recommends that these groups concentrate on the more central themes in order to avoid dispersion, and /or that the members of these groups merge, and thereby reinforce the other teams of the Unit or other Unit more in line with their interest, in order to better align and improve their scientific potential. This is particularly important for the university staff that has very heavy teaching loads. Another problem is the -so far- lack of success of candidates presented at the CNRS recruitment. This will be problematic on the long run, as there are already many teaching people. The retirement of several team leaders during the next term has been anticipated, and the unit should be vigilant for good continuity within the teams, proper funding, and in some cases, sufficient renewal of staff and students.

- Data on work produced:

A1: Number of *produisants* (professors and researchers whose names appear in a minimum number of "publications" over a 4-year period) listed in N1 and N2 in the project column	27
A2: Number of *produisants* among the other staff listed in N3, N4 and N5 in the project column	14
A3: Proportion of *produisants* in the unit [A1/(N1+N2)]	1
A4: Number of theses for accreditation to supervise research defended	1
A5: Number of theses defended	24

3 • Specific comments on the research unit

- Appreciation on the results

The relevance and the originality of the research conducted is attested by the very good publication records of the different teams. 130 publications in journals with good to high visibility, half of these in Journal with an IF >4. The partnership between the university , the INSA and the CNRS is classical, the association with Bayer CropScience is more original and works very well, for the benefit of all partners.

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

This is variable for the different teams, but they are at least fairly active and recognized at the national level, and in general at the international level. As many university based units, they attract a lot of students As mentionned above they are fairly efficient in terms of external funding, with a 4 fold increase during the last term. The association with Bayer is also very relevant and allows the rest of the unit to have access to a platform mostly financed by the industrial partner. They are part of two national networks (Legionella and Genolevure).

- Appreciation on the strategy, governance and life of the research unit

The unit organization is simple and efficient, with a laboratory council and a Direction Committee. The latest gathers the heads of the different teams twice a month, and take all urgent decisions and make adjustments. From the discussions with the different socio-economic classes (Researchers, ITAs (technicians/engineers/administrative and students/postdocs), everyone seems happy with the organization, with a few minor points reported such as a need for higher frequencies of lab meetings for one team (students), the need for a unified database to manage finances from the different relevant organisations (ITA). The relevance of initiatives aimed at scientific coordination, emergence of cutting edge projects and taking of risks are good, with the restrictions detailed in the teams reports. The involvement of the unit's members in teaching activities and in organizing research at the local level is a characteristic of the UMR, more than half of its staff scientists (18 persons) have (heavy) teaching duties and are involved in different university programs.

- Appreciation on the project

With the restrictions detailed in the teams reports, the projects are relevant and feasable during the next term of the unit life. All the projects are originals, though to different extents as detailled in the team reports and for a few case they could be slightly more ambitious. Among the projects, several are risk-taking but this is clearly justified apart from the specific case of the team 2 project, where concerns have been expressed by the committee.

4 • Appreciation team by team

Team 1: « Facteurs de virulence de la bactérie phytopathogène *Erwinia chrysanthemi*».

Team leader : N. COTTE-PATTAT

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	2	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	4	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	2	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2,1	1,7
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	7	7
N7: Number of staff members with a HDR or a similar grade	5	3

- Appreciation on the results

The team has a long standing expertise in the study of the secretion of virulence factors by the phytopathogenic bacteria *Erwinia chrysanthemi*. Two type II secretion systems were studied in detail and the structure of their substrates was determined. The team was also implicated in genomics of *Erwinia* and has undertaken a systematic study of regulators of the LacI family. Different regulatory networks were also studied. The work achieved is of high quality and the many publications (32 in the considered period) attest to the impact and relevance of the results.

In the past four years, the team has a good publication track record wih 32 peer-review publications in good to excellent journals of the speciality (J. Bacteriol (5) ; Mol Microbiol (3) ; Mol Plant-Microbe Intera (2) ; Appl Env microbiol (2); J Biol Chem (3); EMBO J (1) ; Microbiology (1)). 11 masters students were trained and 7 students have sucessfully defended their PhD thesis. Most PhD are now on a postdoctoral stay. Members of the group were implicated in organizing national conferences.

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

Members of the group were invited to one international and one national conference and have presented several posters at national and international conferences Concerning the Ability to recruit top-level scientists, post-docs and students, and more particularly from abroad, the success is quite limited. This could become problematic on the long run, especially with regard to the necessity to attract excellent candidates to be presented for recruitment. This is critical to ensure renewal and vitality for the next term.

The team has sucessfully obtained funding for many competitive calls in many national and one international program.The committee appreciated the international visibility of the team in the field of protein secretion and the presented projects on the molecular mechanisms of type II, which capitalize on a strong in-house experience and excellent collaborative networks.

- Appreciation on the strategy, governance and life of the research unit

The unit members seem to be very happy and the organization and internal communication works well, however the organization of regular internal labmeetings would be appreciated by the younger unit members. The team is motivated and takes many different initiatives to build up the project. Two of the six permanent scientists have teaching responsabilities at the University at different levels including organizing coursework.

- Appreciation on the project

The presented project is a general continuation of the themes developed by this group on type II protein secretion but also the development of new topics. The projected reorganization of the team should not affect its scientific productivity. Team 1 will continue to study bacterial virulence mechanism in the *Erwinia* model, introducing comparative genomic tools to identify new virulence loci. Part of the team will follow up on a recent observation that *E. chrysanthemi* can also infect aphids. While the committee expressed concerns about the biological relevance of this biotic interactions, it nevertheless considers that the use of this new model could potentially reveal new aspects of Erwinia relationships with its host(s). The project on *Erwinia*-insect interactions is quite original and risky, the type II secetion studies are very interesting but more classical.

- Conclusion

– Overall appreciation

The group is composed of a very motivated team with six permanant scientists and many students. This group has an international reputation in the study of type II secretion in *Erwinia* and has good national and international collaborations. The team was sucessful in obtaining good funding from several sources.

– Strengths and opportunities

Very productive association of CNRS and University researchers leading to a good national and international visibility for a group considered by the committee as very competitive in its field. Very good level of external funding and good publication records. The high number of PhD students supervised in the unit speaks for the attractiveness of the team

– Weaknesses and threats

Considering the former excellent scientific cohesion of the group, the management of the unit should carefully accompany the progressive diversification of the research projects within team 1.

– Recommendations

The development of these new reseach axis will increase the need for regular intergroup lab meetings to maintain the cohesion of the unit. The committee recommends the reinstauration of regular laboratory meetings as part of the formal training of the students.

Team 2 : « Structure de la chromatine et dynamique des réseaux de régulation de la virulence ».

Team leader : H.W. Nasser

This new team gathers a former sub group of team 1 and scientists of the former team 3 (biofilms), 2 sub-projects

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	1	3
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1,2 ETP	1,9 ETP
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	5	3
N7: Number of staff members with a HDR or a similar grade	2	4

- Appreciation on the results of the former groups and team

The group from former team 1 has a recognized expertise in the field of regulation in *E. chrysanthemi*. They have been able to get several contracts with good fundings (ANR blanc, BQR, CNRS). The former team 3 had a long standing international recognition in the biofilm area, but they faced different problems during the last term, mostly to attract funding to pursue the application of their finding on the anti-biofilm process.

The group from former team 1 (H.W. Nasser) had a good publication production, with 17 articles during the last 4 years, in the leading journals of their speciality (Mol Microbiol, J Bacteriol, Env. Microbiol. J Biol Chem,and 2 PhD thesis). The former team 3 produced 10 articles in leading journals of microbiology (J. Bacteriol., Microbiology, Res. Microbiol.), and 3 Phd thesis.

2 collaborations are established around grants already received, and a collaboration with other partners is planned, with teams involved in bacterial nuclear structure, regulatory network modelling, and virulence and adhesion.

Concerning the project on Non-coding RNA conduct by one researcher, collaborations are in progress within the unit (proteome platform) and on the Univ. Lyon campus, and also with Institut Pasteur and Genoscope.

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

They have several PhD students. The Ability to raise funds is good, they have been able to get several national grants as a coordinator (ANR Blanc 2008-2010 ; BQR INSA 2009-2010 ; MIE CNRS 2007). Two other grants were obtained by the former team 3 members as parners (ANR alimentation et Nutrtion humaine 2005, BQR université Lyon 1 2006) 5 collaborations are being initiated with teams involved in bacterial nuclear structure, regulatory network modelling, and virulence and adhesion. In some cases, joint grant proposals have been filed.

- Appreciation on the strategy, governance and life of the research unit

Of the 5 staff scientists, 4 have teaching duties.

- Appreciation on the project

A new team is being created by members of "old" teams 1 and 3. While team members clearly make use of their individual expertise and in at least two examples have published in the area of the future work, the project forges into new research areas concerning chromosomal architecture and gene regulation, as relevant to bacterial virulence. The group proposes to use novel technologies, mathematical modeling, and high-powered microscopy to address these broad questions that will need to be defined experimentally. A small group associated with the team is undertaking the study of non-coding RNAs in Agrobacterium tumefaciens.

The main project is based on the importance of chromosomal architecture on gene expression. A main aim is to understand how factors dictating DNA state, such as the "histone-like" proteins H-NS and Fis, impact on virulence, by examining global DNA states under different growth conditions. Studies will be performed in Erwinia chrysanthemi (aka Dickeya dadantii), a phytopathogen (and as discovered by their previous team's results, an insect pathogen). The proposed sophisticated approaches include Surface Plasmon Resonance Imagery and Coimmunoprecipitation of chromatin (Chip) to study roles of H-NS on gene expression, and Atomic Force Microscopy and Laser footprinting to examine transcriptional initiation in the presence of specific regulator-promoter couples. The objectives are to determine which genes are co-coordinated, when at least one of the genes is known to be implicated in virulence. The project will further combine mathematical modeling and genetic studies using reporters to follow expression.

The researchers have previous experience (using known genetic approaches) in regulatory networks via studies of global regulators and structure-functional studies, and among their collectively 27 publications of the last 4 years, have addressed questions on Fis and virulence. The use of highly global approaches was presented as being central to the principal upcoming project. The proposed project is in a highly challenging and open field. In view of the complexity and vast research area of the project, it is advised that participants i) define the specific questions they intend to start with, with manageable objectives and clear experimental questions, and ii) make clear the part of the work involving their expertise and how it fits with those of their partners. Some of these aspects were not clear in the presentation. Team members came willingly to discuss these questions more fully with the committee, but time was insufficient.

An another project conducted by one researcher aims to identify non-coding RNAs in plant symbiont and pathogen Agrobacterium tumefaciens. Prediction and deep sequencing will be followed by a study of conditions that lead to ncRNA expression, and finally a search for their regulated partners.

There are some concerns on this project: 1. The group working on this project is essentially alone on A. tumefaciens (the rest of the team is working on E. chrysanthemi), and involves a single researcher with teaching responsibilities, part time ITA, and one student. It seems that a stronger team dynamics would have been formed in this situation by focusing on a single organism (E. chrysanthemi). 2. While identifying ncRNAs has become feasible by bioinformatics and deep sequencing, the steps following identification, i.e., 5' and 3' mapping, identifying target RNAs, and finding biological functions, are time-consuming and require deep studies. It seemed from the report and presentation that the team underestimates the complexity of identifying targets: while in progress proteomics (by pulse labeling) is a useful approach, more direct techniques (e.g., short-pulse transcriptome with conditional ncRNA expression, or target fishing) are important complementary approaches for target identification. Those steps must then be followed by validation steps. To succeed in the project, good planning and a strong collaborative network will be needed to optimize chances of success.

The relation between the 2 groups comprising Team 2 is not stated. It is unclear why both groups do not work on the same microorganism (Erwinia), which would have facilitated collaboration on common regulatory points, and would have allowed for more animated discussions, exchange of tools, and joint publications.

Although there are publications on the subject of genome organization and virulence, the field is still open, particularly in the application of physical methods. The researchers involved will need to invest in the acquisition of novel techniques and physical approaches. Adaptation of the proposed techniques if successful, could provide important contributions to the field. The ncRNA field is highly competitive, with much left to do. While the first steps are becoming nearly 'routine', identification of targets is still a highly challenging but difficult area, and exploitation of global approaches (ncRNA studies) involve considerable follow-up studies.

- Conclusion

– Overall appreciation

Team 2's main project is ambitious; it involves the use of several novel approaches to study chromatin structure and its correlation with virulence gene expression. This will involve a strong investment by the team to apply sophisticated techniques, and interpret and validate results. Team members should be vigilant for competition in the field; although competitors are few in number, approaches may be similar. The team is clearly enthusiastic about the project, and has already initiated studies in collaboration. The specific short-term scientific objectives should be well-defined.

The second project is also ambitious, and is being carried out by a small and thematically isolated group. The scope of the objectives is very broad and there is some concern about the possibility of obtaining scientifically meaningful results when attacking such a vast project.

– Strengths and opportunities

Team 2: The main project is in an exciting and still very open field. The team members are enthusiastic, and have established good collaborations. The team's scientific expertise in regulatory networks in *Erwinia* should provide a useful base in asking pertinent questions. The creation of a new team with highly experienced scientists with a wide range of know-how provides an impetus and dynamics to the project.

The study of ncRNA could provide valuable information on gene regulation and potentially on bacterial impact on the host, given that the project leads to an in-depth characterization of specific ncRNAs.

– Weaknesses and threats

The relation between the 2 groups comprising Team 2 is not stated. It is unclear why both groups do not work on the same microorganism (Erwinia), which would have facilitated collaboration on common regulatory points, and would have allowed for more animated discussions, exchange of tools, and joint publications.

Team 2's project relies on methodologies and equipment that seem to be mainly performed outside of their own laboratory. In the absence of durable collaborations, this might limit their autonomy in carrying out the project.

Project of 2b team is highly ambitious with a reduced workforce, and parts of the project, i.e., target identification for each of the ncRNAs identified may be a major challenge whose difficulty seemed to not be fully appreciated.

– Recommendations

The optimal choice would be for this team to work on the same bacterium. Alternatively, a reorganization might be considered such that the PI should associated with a team working on Agrobacterium, to avoid scientific isolation. If it is not done, weekly team meetings should be set up to encourage scientific exchanges.

Team 2 should assure itself of a durable collaboration for the planned project, with partners that will provide and transfer their know-how to team members. In the long term, they might consider acquiring the necessary equipment to gain autonomy in the work.

To push the field of ncRNAs further will require the use of multiple methods of target identification, rather than only proteomics. Identification of ncRNA functions will require good expertise of the bacterium and its environment. These requirements should be taken into account to insure scientific meaningfulness of results. A shift to the same bacterium as the hosting team, or moving to a team working on Agrobacterium should be considered.

Team 3: « Bactéries et métaux : métabolisme, homéostasie et résistance »

Team leader : A. Rodrigue

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	1	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	1 to be hired
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1,3ETP	0,9 ETP
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	1
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

The team investigates regulation and mechanisms of metal homeostasis and flux in different gram-negative bacteria. Their studies have led to the characterization of Ni and Co transport systems, including comparisons of the « nik » system in *E. coli* and *H. pylori*, and a second system, « rcn », in *E. coli*. Their work extends to applications, in which bacteria are developed as « metal traps » that could be used as a strategy to de-pollute highly metal-contaminated areas. Their studies also involve metagenomic approaches in ground microbiota to find novel genes involved in metal homeostasis and resistance.

In collaboration with former Team 3, the team determined that intracellular Ni concentrations affect expression of a surface appendage called curli that is needed for biofilm formation.

These studies are relevant and interesting, and the vigilance for applications makes the work attractive and funded.

9 publications, in microbiological journals (J. Bacteriol (2); Applied Envi Microbiol (1); Res Microbiol (1), BMC research notes (1); J Appl Microbiol (1) biochemical (Chem Commun (1); Biochimie (1), and biotechnological (Appli Microbiol&Biotechnol (1).

3 invited talks, 3 talks, 7 posters

3 thesis students (2 completed, 1 in progress)

4 M2, teaching responsibilities

4 collaborations that seem to be successful, as they are the basis for research contracts, and reflect internal collaborations giving rise to copublications.

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

Members of the group were invited to 2 international and 1 national conference and have presented several posters at mostly national conferences. The team has sucessfully obtained funding in national program, including 1 ANR. Whereas international visibility could be improved, the committee appreciated the collaborative network of the team, especially with Indian partners

- Appreciation on the strategy, governance and life of the research unit

One of of the two permanent scientists is teaching at the University at different levels and is implicated in organizing teaching at the University.

- Appreciation on the project

The research project further develops the ongoing scientific work. Team direction will change hands, apparently harmoniously. The team proposes to continue characterizing present and novel systems of metal resistance, and to examine bacterial global responses to metals. Applications that are currently being considered aim at detoxifying metal-polluted areas, by i) using a microbiota approach to identify new genes from metal-contaminated sites, and ii) developing tools (based on genetic identification of metal-responsive genes) to serve as metal biosensors.

The project report was missing a literature search, which would have been valuable for placing the subject in a competitive context. The project might benefit by enlarging its considerations, i.e., going further on questions of impact of metals on numerous biological processes; this might occur naturally by their future examination using global techniques.

The project is well thought out, and could provide important information on how metals are managed intracellularly; the link between fundamental and applied science could feed into several research areas (such as their demonstration of the role of nickel on Curli). Studies on metal-binding systems are performed in numerous laboratories and should be taken into account. A search for new metal transport systems in high-metal environments might lead to identification of previously unknown systems and important applications, although to date none have been identified. More risk-taking, e.g., by extending questions towards other fields, would enrich this solid project. The future project includes the use of global methods, and metal-sensors, which may lead the team to broaden the scope of the project.

- Conclusion

  - Overall appreciation

The team is well-focused on the specific question of metal transport and toxicity in bacteria. It gains relevance by considering socio-economic applications. Taking 'scientific risks' by delving further into the roles of metals in bacterial processes, and by extending collaborations was not discussed due to a lack of time, but such measures might enrich this already solid project.

  - Strengths and opportunities

Team is well-focused with clear expertise in an ecologically relevent field. Applications are considered and pursued, and metal transport systems from different microbiota ecosystems are being searched. The impact of metals on essentially all cell processes opens the door to development of novel areas of research that could extend the scope of the present work.

  - Weaknesses and threats

The team seems to have well identified its area of expertise. It should be vigilant for other teams working in the same area, and be more aggressive in establishing collaborations.

  - Recommendations

The team should consider broadening the scope of the questions being asked. It should be more ambitious in terms of journals in which they publish. They might consider broadening their collaborations.

Team 4: « Mécanismes de virulence et de multirésistance chez Legionella »

Team leader : P. Doublet

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	4	4+1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	3	4
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	3	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	6	5
N7: Number of staff members with a HDR or a similar grade	5	5

- Appreciation on the results

The group "Mécanismes de virulence et de multi résistance chez Legionella" was created in 2005. This team started a new project focussing on Legionella pneumophila, an environmental pathogen. Thus most of the work in the past four years was dedicated to set up methods relevant for studying L. pneumophila, a pathogen not easy to manipulate. The research project investigates different virulence strategies of L. pneumophila and diversity of its eukaryotic host in the environment. The virulence studies are following a classical approach; the environmental study is original and has a good potential to give this group a specificity in a field which is less competitive but very important in Legionella research.

The team was recently created. A first article was published (Plos One) this year and a student will defend his thesis this year.

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

Implication in the organisation of two national conferences on Legionella.

The group was successful in obtaining 8 national and 3 industry funded grants. Except two grants that are finishing this year, all grants are finished.

Participations in several national networks

- Appreciation on the strategy, governance and life of the research unit

The organization and internal communication works well as stated by all the team members.

The team is motivated and takes many different initatives to build up the new project.

Five of the seven permanent scientists have teaching responsibilities at the University at different levels and are implicated in organizing masters courses at the university.

- Appreciation on the project

The proposed research project is a general continuation of the themes developed during the last 4 years dealing with specific virulence factors of Legionella and by investigating the environmental protozoan reservoir of Legionella. The project should lead to interesting new results, but the group has decided to focus on very competitive questions in a very competitive field with many excellent groups around the world and sometimes also on difficult models to set up. The virulence projects follow classical approaches and the project on the environmental protozoa has good potential of giving this group a specificty in the Legionella field and should also lead to new results needed to better understand the biology of Legionella in the environment.

The project on enviromental amoeba is quite original; the virulence studies are very interesting but more classical and risky with respect to international competition.

- Conclusion

  - Overall appreciation

The group created 4 years ago is composed of a very motivated team with seven permanent scientists and many students. In the last four years they have set up many completely new techniques, collaborations and projects on L. pneumophila a pathogen nobody has worked on before in the unit. The topics are interesting but very vast and very different aspects of Legionella research are tackeled.

  - Strengths and opportunities

The strength of the team is their motivation and good atmosphere which allowed it to successfully set up many different methods during the last years to work with Legionella. In particular the environmental project on the host of Legionella might give this group an opportunity to find its specific niche that is in addition less competitive than the other topics studied.

  - Weaknesses and threats

The weakness of the teams lies, for us, in the very many and diverse projects that have been started during the last years and the many different projects planned. This might lead to dispersion and to difficulties for publishing in good journals.

  - Recommendations

The team is in a good position to build up a competitive group woking on Legionella in France. We recommend to putting more emphasis on the environmental project on amoeba and to focus the overall research projects and goals of the next four years on fewer subjects and methods. The establishment of international collaborations is also recommended.

Team 5: « Génétique Moléculaire des levures »

Team leader : M. Lemaire

- Staff members (on the basis of the application file submitted to the AERES)

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

- Appreciation on the results

The team develops a high quality genetic approach to study glucose metabolism in *Kluyveromyces lactis.* This organism is a good model to obtain a better understanding of the regulatory network governing glucose metabolism. It possesses two advantages compared to the classical model organism *Saccharomyces cerevisiae*: i) its genome is not duplicated and ii) its glucose metabolism is more similar to what is found in multicellular organisms. The team also participates in the "Genolevures" consortium and one of its members is involved in yeast prion analysis.

Most publications during the last four years correspond to collaborations on other projects, mainly those developed by a member of the team recruited in 2005. Best-cited publications correspond to "genolevures" reports on yeast genomics. Publications directly dedicated to the main project are produced and published in journals with high visibility in Genetics and microbiology (Genetics, Mol. Microbiol., Eukaryo. Cell). This research has a good visibility in the field, which is attested by the fact that these publications are well cited (competitive with those from other groups in their field). The group contributed to training of master and PhD students (3 master students training and two theses during the last 4 years).

The team developed two collaborations with international partners that have both led to joint publications. The team is a historical partner of the Genolevures consortium which holds a major contribution to the field of yeast genomics which pursue high impact research on comparative genomics of yeasts.

During the last contract, one post-doc and 2 invited professors have spent short periods in the group. The team has contributed four communications in international meetings. The team has recruited a "maître de conférences" (associate professor) during the last contract period and an associate professor has been promoted to a professor position. Currently, there is no PhD student or post-doc in the team. The team is stable: a Pr will retire and is not involved in the next contract period, but a new associate professor will be recruited next year.

The abililty to raise funds constitute the weakest aspect of the team's achievements. This point should be improved for the team to survive.

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

The organization, management and communication policy of the team raise no problem and are well adapted to the general organization of the unit. Both the project leaders and staff scientist are deeply involved in teaching.

- Appreciation on the project

The project is aimed at continuing the analysis of glucose metabolism in K. lactis. The basic science behind is sound and interesting but the project will be feasible only if funds can be raised.

There is a lack of ambitious projects. The team would benefit to use its very good insertion into the Genolevures consortium to develop projects with broader objectives. For example, comparative genomics directly dedicated to the deciphering of glucose metabolism regulation may open new research directions. Similarly, several techniques already in use in the group (chromatin IP is one of these) if used at a higher scale could be the source of new candidate genes or mechanisms. Developping such high throughput projects would also probably help to get funding.

- Conclusion :

  - Summary

The team develops very solid basic science in the field of yeast genetics and genomics to decipher the regulation of glucose metabolism. Although all members are teachers and deeply involved in teaching administration, they keep a correct level of publication.

  - Strengths and opportunities

The participation in the Genolevures consortium is a very positive point, for the increased access to recent scientific information, collaborations, and joint publications of high standing.

  - Weaknesses and threats

Despite the quality of their work, the team experienced difficulties to obtain substantial funding during the last years, which had several negative impacts on the team achievements. More generally the small size of the group might be compensated at least in part by developing internal collaborations; in this respect the next 4 years will be critical.

  - Recommendations

More ambitious projects would increase the visibity of the team and help obtaining grants. In that respect the recruitment of the new associate professor will be an opportunity to get the complementary expertises needed to reach this goal. The ability to succeed in competitive fundings will guarantee the viability of this team.

Team 6: « Génomique fonctionnelle des champignons pathogènes des plantes »

Team leader : N. Poussereau

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	4	4
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	4	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	8	5
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	3,8 ETP	3,8 ETP
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	2	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	3	5
N7: Number of staff members with a HDR or a similar grade	7	6

- Appreciation on the results

The research of this group focused on the functional genomics of plant pathogen fungi and in this frame the group has a very effective link with the private company Bayer. Over the past four years, the team has made a strong and time-costly investment in developing and exploiting genomic resources. The team encompasses two main research programs. The first one is devoted to the identification of the molecular mechanisms involved in the infectious process of two fungi of economical importance exhibiting different pathogenicity strategies: the hemibiotroph fungus *Magnaporthe grisea* and the necrotrophic fungus *Botrytis cinerea.* The objective is to identify new targets for developing fungicides with large spectrum. The other project is focused on the seed vigour which directly impacts the quality of seed germination. This team has developed an efficient platform shared with Bayer Crop Science.

The team has been very productive (41 primary and 15 collaborative publications), with publications in the top journals in the field (PNAS / Plant Cell / Plant J. / Plant Physiol). Of note the training of 13 PhD represents a very dynamic part of the life of the team.

The research of this group focused on the functional genomics of plant pathogen fungi and in this frame the group has a very effective link with the private company Bayer.

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

Three post docs were/are present over the past four years showing the attractivity of the group.

The ability to raise funds and to successfully apply for competitive funding is excellent with 2 ANR Blanches; 2 Génomique microbienne/Génoplante; 2 bi et tri-lateraux Génoplante; 1 Marie-Curie European fellowship.

In addition this team has a good integration in collaborative international networks on fungi and leads a national fungi network.

The outcome is very good with four patents among which three are in the process of patent extension.

- Appreciation on the strategy, governance and life of the research unit

The organization of the team is efficient and dynamic with good interactions with researchers from the private company Bayer Crops science. The team is motivated and takes many different initatives to build up the project. The present team leader will move soon to another institute. The new team manager will be facing important challenge with the new project and the UMR director and Bayer CropScience should facilitate this transition.

- Appreciation on the project

The project for the four coming year is ambitious, focusing mainly- and it is a very good point- on the first step of the plant-fungi interaction. It should deliver an interesting view on the functional aspects of infective processes of two fungi showing very different life styles (Hemibiotrophic versus necrotrophic). Based on the resources already developed they can expect the best output from their biological models.

The team has to pursue the very effective link with the private company Bayer on identification of putative new targets for fungicides and on fungi detoxification mechanisms. In this frame, the proteomic plateform constitutes an important tool for the collaborative aspects. In addition all these projects are well supported by CIFRE grants, exhibiting the great interest of the private compagny for this project.

The localisation of the team in the research center of Bayer CropScience is another very good point that will ensure effective links between fundamental and finalised researches.

- Conclusion

– Overall appreciation

This team has shown an effective and fruitful collaboration with the research department of Bayer CropScience. In spite of the abundance of the topics treated, it represents a very good research team, well financed and productive, with very good record of publications and tutoring of PhD students.

– Strengths and opportunities

They develop original and efficient combination of approaches to decipher the contribution of different pathways in plant fungal interactions. In that respect the comparison between two fungi showing different life-styles is of interest to identify new fungicides with very large spectrum. In regard to the size of the team and to the closely links with the private company this team has an original position in a competitive field and on the leading edge of that field.

– Weaknesses and threats

The present team leader will move to another institute in the next two years and the size of the team will slightly decrease. A new team leader has been designated for the next four years. The UMR director and Bayer CropScience should accompany the management of the team during the next months/years, to support the group leader in her new responsibilities.

– Recommendations

The project needs to be focused as it is stated in the presentation e.g. on the first step of the plant-fungi interaction. The team will keep on the development of their original and efficient combination of approaches to decipher the contribution of different pathways in plant fungal interactions.

Note de l'unité	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	B	A	A

Nom de l'équipe : FACTEURS DE VIRULENCE DE LA BACTÉRIE PHYTOPATHOGÈNE ERWINIA CHRYSANTHEMI

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	A	A	A

Nom de l'équipe : MÉCANISMES DE VIRULENCE ET DE MULTI RÉSISTANCE CHEZ LEGIONELLA

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	B	B	A	A

Nom de l'équipe : GÉNÉTIQUE MOLÉCULAIRE DES LEVURES

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	B	A	A

Nom de l'équipe : STRUCTURE DE LA CHROMATINE ET DYNAMIQUE DES RÉSEAUX DE RÉGULATION DE LA VIRULENCE

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	A	B	B

Nom de l'équipe : GÉNOMIQUE FONCTIONNELLE DES CHAMPIGNONS PATHOGÈNES DES PLANTES

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A+	A+	A+	A	A+

Nom de l'équipe : BACTÉRIES ET MÉTAUX : MÉTABOLISME, HOMÉOSTASIE ET RÉSISTANCE

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	B	A	A

Université Claude Bernard Lyon 1

Le Président
Lionel Collet

Villeurbanne, le 13 Avril 2010

M. Pierre GLORIEUX
Directeur de la section des unités de l'AERES
20 rue Vivienne

75002 PARIS

Monsieur le Directeur,

Je vous remercie pour l'envoi du rapport du comité de visite concernant l'unité de recherche :

«Microbiologie, Adaptation et Pathogénie» rattachée à mon établissement.

Ce rapport n'appelle pas de commentaire particulier de la part de l'université.

Je vous prie de croire, Monsieur le Directeur, à l'expression de ma meilleure considération.

Le Président de l'Université

Lionel Collet

Microbiologie, Adaptation & Pathogénie
CNRS UMR 5240
Université Lyon 1
INSA de Lyon
Bayer CropScience

Answer to the AERES evaluation report

We thank the members of the visiting Committee for their evaluation and recommendations. We would like to add a few precisions on some specific points raised on the UMR or the teams.

Concerning the geographical dispersion, the unit is located on two nearby sites. It is of prime importance for Team 6 to closely interact with Bayer CropScience. It is also a benefit for the UMR with shared equipments and platforms.

The director and the Laboratory Council consider that the teams are coherent in their scientific objectives and approaches even if they use different models. Moreover, the recent implementation of two transversal axes in the unit will favour exchanges between the teams. In the proposed organisation chart, an emergent project was associated with Team 2 to avoid the isolation of this novel topic in the UMR. This presentation has clearly interfered with the visibility of the project of Team 2 which is a coherent group centred on transcriptional regulation. The emergent project, separately proposed by a young scientist, deals with a biological question matching the UMR scientific priorities; it was supported by both the UMR and CNRS. However, the UMR has previously considered that the status of this emergent project should be evaluated after a trial period; this management fits with the Committee expectations.

Efforts of recruitment will be pursued. To this end, one candidate is presented to CNRS this year and others are planned for the next years.

Team 1: « Facteurs de virulence de la bactérie phytopathogène *Erwinia chrysanthemi*».

Recruitments, at different levels, remain a priority for the group. During the four past years, candidates applied for a CNRS position, but unsuccessfully. However, the group regularly recruits PhD students; during the last term, about half of them were from abroad, showing the team attractiveness. The decreased team size will favour the organization of regular internal meetings which are important for the training of PhD and Master students. As previously, the unit management will take care of the cohesion by accompanying the diversification of the research projects.

Team 2 : « Structure de la chromatine et dynamique des réseaux de régulation de la virulence ».

We would like to precise that concerning the emergent Project “ARN non codants”, such a chart organization was decided by the UMR Council to show that this new project could benefit of scientific interactions with Team 2.

We noticed some errors in different sections of our evaluation: staff members, number of publications of the researchers from the former Team 1 (17 instead of 11), role of the team in the funded projects since in most cases, we were coordinator and not only partners (ANR Blanc 2008-2010, BQR INSA 2009-2010, MIE CNRS 2007 and recently, PICS CNRS 2010-2012). It appears to us particularly important to underline our major role in structuring research projects.

Our project is structured around a central question: how do nucleoid associated proteins rationalize chromatin structure and virulence gene expression in response to environmental and physiological conditions? This central question was declined in the project document (page 22 to 23) and in our oral presentation, in four points which will be performed in the following chronology: (1) how are the different *pel* genes responsive to environmental and physiological conditions known to modulate bacterial virulence and to affect the DNA supercoiling state? Are other virulence genes co-regulated in a same way? (2) Does virulence gene expression involve alterations of the template properties of chromatin? (3)

Role of the “histone-like” proteins H-NS and Fis in nucleoid structure and virulence gene expression? Macromolecular assembly during control of virulence gene expression? (4) Dynamics of regulatory networks associated to virulence.

We are aware of the complexity of our project. However, most of the tasks are conducted in the frame of funded projects. In these projects, we will provide our expertise in the study of gene expression in *E. chrysanthemi* and in genetics and physiology of this pathogen, while our collaborators will bring their expertise in the study of nucleoprotein complex formation and in global regulation of gene expression by DNA supercoiling state.

About competition, there is, to our knowledge, a unique group working on bacterial DNA topology and infectious disease. This group concentrates its activity on the expression of *Salmonella* secretion systems and does not analyse the global coordination of gene expression in response to changes in DNA supercoiling. Our work is clearly complementary to that of this group since their model is an animal pathogen. Concerning external collaborations, we have already worked with scientists of different expertises (chemists, crystallographs, mathematicians…). In the case of our novel ANR project (Damage, 2010-2012), a scientist from our group will be trained in a collaborator laboratory to implement within Team 2 the SPRi and photofootprinting technologies required for further investigations

Emergent project : « ARN non codants et adaptation des bactéries à leur environnement »

The Committee underlined both the ambition of this project and the small size of the group. This emergent project was recently supported by CNRS with a PEPS grant and by a complete teaching discharge for the PI, showing a positive scientific evaluation. Concerning the biological question (How can bacteria switch from free-life style to interactions with eukaryotic host?), we retained the most appropriate organism as its free-life style and its interaction stages are very well documented. The group potential is already improved by a full-time technical assistance and a collaborative network. A fruitful collaboration exists on the bacterial model with a local team (common ANR and PhD student). In association with this team, an ANR JC covering the project has been submitted this year. New collaborations will also be developed on ncRNA domains. The project will clearly benefit of the UMR platforms and organization in axes. Since projects on ncRNA analysis also interest Bayer CropScience, the opportunity to extend this collaboration in the frame of Team 6 will be considered. For the identification of ncRNA targets, the methods proposed by the Committee (transcriptomics and proteomics) fully match those described in our report and oral presentation.

Team 3: « Bactéries et métaux : métabolisme, homéostasie et résistance »

Good note has been taken to follow on our efforts in establishing new collaborations, which is already the case through participating in a national network on biosensors and beginning an international collaboration with Spanish colleagues on nickel homeostasis. We are fully aware of the international competition in our field which is high and which has led in the past to some difficulties in publishing our data. Broadening the scope of our work is an answer; it has already started (proteomics on *P. putida*, metagenomics) and will be pursued.

Team 4: « Mécanismes de virulence et de multirésistance chez Legionella »

Team 4 thanks the Committee for his support to this new group and new project. Concerning the risk of dispersion, the team will focus on more limited subjects after the defence of the three ongoing thesis and publications of the corresponding results. The team agrees with the good potential of the environmental aspect, particularly considering the weaker international competition in that field. This readjustment has already been taken into consideration with the recruitment this year of a new Associate Professor whose work will be dedicated to analysis of environmental hosts (amoeba and protozoa) of *Legionella*. For the next four-year period, the team will focus on the mechanisms required for the intracellular life of *Legionella* in the environment.

Team 5: « Génétique Moléculaire des levures »

We are pleased by the Committee’s evaluation, especially regarding the quality of our scientific approaches. However, we disagree with the Committee in that we would like to stress that our projects are ambitious, for they are focused on innovative aspects of glucose signalling (genesis of glucose signal, connection with glycolysis). Moreover, we consider ambitious the start of a very recent research program at the biology-chemistry interface (mentioned during the presentation) that has already been supported by the allocation of a PhD CNRS fellowship. Finally, we do agree that important efforts have to be invested in the parallel development of a global approach in order to be able to raise funds. In that respect, we are

planning to recruit this year an Associate Professor whose profile meets the requirements necessary for the realization of such an approach.

Team 6: « Génomique fonctionnelle des champignons pathogènes des plantes »

Team 6 is grateful to the evaluation Committee for his overall positive opinion of the team's dedication to both the development of a fruitful collaboration with our industrial partner - including that of a common proteomic platform - and that of a competitive research on plant fungal interactions. With respect to the Committee comment about the change of the team leader, the Team 6 members, the UMR director and Bayer CropScience reiterate their strong support to the novel team leader for the next four years. Besides, the team fully agrees with the Committee to focus on the early steps of the infection process, as it was presented in the Team 6 project. The collaboration with the research department of Bayer CropScience will continue to be strengthened and we hope further developed.

Villeurbanne, le 09 Avril 2010

Nicole COTTE-PATTAT
Directrice de l'UMR5240