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

Section des Unités de recherche

Evaluation report

Research unit

Microbiologie et Génétique Moléculaire

AgroParisTech



June 2009



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et de l'enseignement supérieur

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Evaluation report

Research unit

Microbiologie et Génétique Moléculaire

AgroParisTech



Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

June 2009



Evaluation report



The research unit :

Name of the research unit : Microbiologie et Génétique Moléculaire

Requested label : UMR_A INRA, UMR CNRSCNRS

N° in case of renewal : INRA 1238 - CNRS 2585

Head of the research unit : M. Jean-Marie BECKERICH

University or school :

AgroParisTech

Other institutions and research organization :

INRA

CNRS

Date of the visit :

December 3, 2008



Members of the visiting committee

Chairman of the committee :

M. Bernard DUJON, Institut Pasteur, Paris, France

Other committee members :

M. Jean-Marc GHIGO, Institut Pasteur, Paris, France

M. Carlos GANCEDO, Instituto de Investigaciones Biomedicas, Madrid, Spain

M. Jörg STÜLKE, Institute for Microbiology and Genetics, Göttingen, Germany

Ms. Carol MUNRO, University of Aberdeen, United Kingdom

CNRS, CNECA and INRA representative :

Ms. Bénédicte MICHEL, CoNRS representative

M. Vincent MARECHAL, CNECA representative

M. Christian BOUCHER, CSS INRA representative

Observers

AERES scientific representative :

M. Stéphane MERESSE

CNRS representative :

M. Miklos de ZAMAROCZY

INRA representative :

Ms. Emmanuelle MAGUIN



Evaluation report



1 • Short presentation of the research unit

The unit comprises 6 teams. At the date of the evaluation, the unit included 50 persons, 38 having a permanent position. The overall staff distribution was :

- 6 Professors and Assistant Professors, 3 having an HDR (or the equivalent)
- 17 researchers (14 INRA and 3CNRS), 7 having an HDR (or the equivalent)
- 2 postdoctoral fellows
- 15 ITA/IATOS
- 9 PhD students, all paid by fellowships. 11 students have defended their thesis between 2004 and 2007.

2 • Preparation and execution of the visit

8h30	Meeting of the committee in private audience
9h00	Discussion with the direction of the laboratory
9h30	Hearing of research group 5
10h20	Hearing of research group 6
11h10	Coffee break
11h30	Hearing of research group 1
12h10	Hearing of research group 2
12h50	Lunch
14h00	Hearing of research group 3
14h40	Hearing of research group 4
15h20	Meeting with the staffs
16h00	Coffee break
16h20	Meeting with the CNRS and INRA representatives
16h40	Discussion of the committee in private audience



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

According to the policies of its several host Institutions, the « Microbiology and Molecular Genetics Unit», performs basic research on the physiology of microorganisms with a choice of topics and organisms selected according to possible applications in the fields of biotechnologies and food safety. The fact that the teams of this Unit will join the MICALIS program will profoundly modify the research activity of the Unit, and it was not always clear to the committee how some scientific themes will be successfully incorporated and can be productively developed in the future.

4 • Specific appreciation team by team

Team: Physiology and Genetics of Bacteria

This team works on protein phosphorylation as a mechanisms of regulation using, historically, *Bacillus subtilis* as a model and now several other bacteria. Two major mechanisms are studied: the phosphoenolpyruvate-dependent phosphorylation catalyzed by the PTS, and the ATP-dependent phosphorylation. A new scientist has recently joined the team and further reinforces its scientific potential on this important topic.

The committee was impressed by the quality of the work and wishes to stress that the team leader is the best recognized world specialist about PTS, inspiring numerous collaborations. The list of publications is impressive and, even though many of them reflect the collaborations, several important ones represent the quality of the work of the group itself.

Nom de l'équipe : Physiologie et génétique des bactéries à GRAM+

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

Team : Regulation and biofilms in Bacilli

This team studies the central carbon metabolism in *Bacillus subtilis*. In parallel, the team started a new research project in 2003 on the study of the molecular basis of biofilm formation in the emerging food pathogen *Bacillus cereus*.

Concerning the studies on the regulation of central carbon metabolism, the committee acknowledges the high quality contributions of the team to this field. The group has published several papers in good and very good journals. The group is involved in many European collaborations, a major initiative is the BaSysBio project that is aimed at the systems biology of growing *B. subtilis* cells. Given the impact of *B. subtilis* as a model organism for all gram-positive bacteria, this activity will undoubtedly be central in MICALIS.

Regarding the study of *Bacillus cereus* biofilm, the committee recognizes that this topic will easily fit into MICALIS, which is already visible through ongoing collaborations with other teams of the future department. However, the committee expressed some concerns with regards to the very low number of publications that



have been produced directly on this subject so far. Although manuscripts are currently in preparation, it is not clear how the different projects presented will lead to approaches significantly original compared to ongoing investigations performed in other biofilm models. A more focused scientific effort is required in the perspective of the creation of a biofilm team in MICALIS.

Nom de l'équipe : Régulation génétique et biofilm chez les bacillacees

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

Team: Comparative genomics of yeasts and molecular typing

The team studies a variety of molecular aspects concerning the evolution of yeast genomes as part of its participation to the Génolevures Consortium of laboratories (CNRS GDR2354) and, at the same time, hosts the Collection de Levures d'Intérêt Biotechnologique (CLIB), now part of the Centre International de Ressources Microbiennes (CIRM).

Studies on yeast genome evolution concerns primarily the analysis of transposons and introns, two topics in which the team specializes, plus a specialization on the diversity of two clades of hemiascomycetes, one containing the salt-tolerant yeast *Debaryomyces hansenii*, often found on cheeses, the other containing *Yarrowia lipolytica*, a long-term model for several teams of the Unit. A yeast intron database has been set up. Although limited to a few species yet, this database has no equivalent elsewhere and should be encouraged.

The team also participated in the genome annotation of the wine yeast EC1118, which revealed an interesting phenomenon of introgression.

The team has a good number of publications with regard to the small number of scientists. Most publications, however, are in specialized journals, if one excepts the publications co-signed with the Génolevures Consortium. The committee was concerned by the number of projects and in particular by their diversity.

The committee was favorably impressed by the renovation of the CLIB and the quality of the service offered to the community. It encourages the team to further develop taxonomy using molecular methods.

Team: Peroxisomes and metabolism of hydrophobic compounds

The team has been working on the subject of hydrophobic substrates utilization in the non-conventional yeast *Yarrowia lipolytica* during the last years with an acceptable level of publications even if there are no articles published in top microbiology journals. During this work, the leader of the team has established a series of collaborations that are useful for the development of the topic. Nevertheless, he should be warned against a too widespread expansion that could jeopardize the concentration on critical points. The use of these substrates produces a development of peroxisomes in the above mentioned organism; however, it is the opinion of the committee that although *Y. lipolytica* may be useful in the study of problems related to peroxisome biogenesis there are already well established yeast systems, e.g *Pichia pastoris*, that could be more useful than *Y. lipolytica* for this question (unless some very specific issue is studied).

The committee appreciated the efforts of the team leader to use the potentialities of the organism under study in industrial applications. The patents obtained reflect promising results in this direction.



It was not completely clear to the committee how the work going on will fit in the future integrated scheme of the MICALIS program. Nevertheless, the work is considered of quality and the new incorporation in the group - not mentioned during the exposition- could bring some intellectual and working help to the team.

Team: Expression and secretion of proteins

The team "Expression and protein secretion" has been involved in protein secretion and quality control in the yeast *Yarrowia lipolytica*. This study also has had implications in the development of efficient vectors for expression of heterologous proteins in this organism; as a result a proprietary kit is currently in the market. Although the scientific production of the team for the past 4 years can be considered as modest, the committee underlines a recognized expertise of this team in the field of protein secretion and quality control in yeast.

A new line of research is being initiated in order to redirect the team towards a better integration in the MICALIS project, namely the study of the biology of cheese ecosystems. At present, the team has been studying the formation of some flavor compounds derived from sulfur-containing amino acids in cheese.

The committee expressed some concerns with regard to the future projects that have been presented. Although it is recognized that the new line is interesting and may produce good results, the committee thinks that it should be clearly focused and more specifically directed. In the present situation, the committee had some concerns for a good level of publication in the future.

Team Signalling and virulence

The "Signalling and Virulence" team members presented their work on the ambient pH response of *Yarrowia lipolytica* and their investigations to determine the contribution of GPI-anchored proteins to *Candida albicans* pathogenesis. The research team has generated a significant number of publications in the period 2004-2008, reflecting a good level of productivity and importantly has established key European-wide collaborations and is internationally-recognised.

The work on *Yarrowia* focussed on endocytic pathway proteins that are involved in the alkaline pH response and in the involvement of the protease Ssy5, a sub-unit of the SPS amino acid sensor complex, in the regulation of the XRT2 gene that encodes an extracellular alkaline protease. The committee will not comment on this research as it will cease in the near future with this part of the team moving to join another group in MICALIS.

The presentation of the *Candida albicans* GPI-protein project was of a high standard and the committee appreciated the importance of the scientific question. The project had clear, defined objectives and the approaches were well constructed with unambiguous rationales. The committee recognised the significant endeavour required to generate such a comprehensive mutant collection and that this will provide a key resource for future analysis. Overall, the GPI-protein research was strongly supported. The committee would like to point out the importance of analysing the GPI-proteins in a range of clinical isolates through collaboration with a group at the Institut Pasteur. They also wanted to reinforce the value of testing these mutants in well-developed models of fungal infections; this was seen as strategic to the main aims of the project. In addition, the development of a model for *C. albicans* commensalism was considered worthwhile and well placed within the scope of MICALIS. Finally, the committee suggested screening the GPI-protein mutant library for alterations in interactions with other microbial species of the human gut microbiota. Examining these interactions would be a very suitable avenue of research that would fit well under the MICALIS umbrella.

Nom de l'équipe : Levure (Fusion de 3 ou 4 groupes non finalisée)

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



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

The unit is well integrated into successful collaborations, including several European programs, and plays an important role in all of them. This provides additional resources to the unit and is scientifically very important for the activity as well as for the life of the unit. Several team leaders are internationally highly recognized in their respective fields of expertise, hence contributing to the attractiveness of the unit. The unit is also highly involved in teaching activities, as is expected for a research unit of AgroParisTech. Numerous PhD students are trained with success and appreciate the mentoring they receive. Very few of them, however, are students of AgroParisTech. Most PhD come from University cursus, or from abroad. The unit maintains high scientific standards and both internal and external intellectual exchanges despite its relative geographical isolation.

6 • Recommendations and advice

— Strong points :

- scientific production of generally high quality, sometimes impressive
- good balance of expertises between bacterial and eucaryotic microbial systems
- important role of the unit in the formation of PhD students
- successful development of the CIRM

— Weak points :

- overdispersion of several scientific projects
- some teams are too limited in size
- scientific priorities too often modified to accommodate institutional demands, limiting originality and performance

— Recommendations :

The committee recognizes the high quality and importance of the scientific production of the unit, the interest of the topics treated, and the variety of scientific expertises accumulated. The committee insists that the major changes imposed to the work of the unit due to its incorporation into the future MICALIS program fit the projects of the most original scientists of the unit.

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	A	A	A

BECKERICH Jean-Marie
Laboratoire de Microbiologie et Génétique Moléculaire
UMR INRA 1238 / UMR CNRS 2585
Mail : beck@grignon.inra.fr

Grignon, July 31st 2009

Answer to the AERES evaluation report concerning MGM

We would like to thank the members of the visiting committee for their time in the analysis of our scientific reports and for interactions with the lab members during the visit, in particular during the hearings of the different groups. We appreciate their overall recommendations and advices but we would like to answer to several specific points raised by the committee.

Team : Regulation and biofilms in Bacilli

The study of *Bacillus cereus* biofilms has been initiated *ex nihilo* in 2003 in a team previously dealing exclusively with transcriptional regulation of carbon metabolism in *Bacillus subtilis*. Several research projects on *B. cereus* biofilms that could contribute to the general objectives of INRA in the food safety field have been started in parallel to identify the more promising ones. This strategy has indeed delayed the publications of the results, which has been noted by the committee. Nevertheless, several original results have been obtained and published, or will be published, in very good microbiology journals: two publications issued in 2006 and 2007 (PMID: 16391139 and PMID: 17169556), one has been accepted in *Appl. Env. Microbiol.* in 2009, one is currently in the revision process for *J. Bacteriol.*, one has just been submitted to *J. Bacteriol.*, and one will be submitted in a couple of weeks.

We agree with the committee's recommendation for the future and, as presented probably too briefly during the evaluation process, the "biofilm" group of the team will develop a very focused scientific project in the coming years.

Team : Peroxisomes and metabolism of hydrophobic compounds

Since the availability of the complete *Yarrowia lipolytica* genome sequence, the team « peroxisomes and metabolism of hydrophobic substrates utilisation » expands its research from studies on peroxisomes and hydrophobic substrates utilisation towards a more global approach as reflected by the new team name « Integrative metabolism of microbial lipid » (Biologie intégrative du métabolisme lipidique microbien).

Several approaches will be used including Xomic analysis (genomics, comparative genomics, proteomics, transcriptomics), system biology and lipidomics to study lipid metabolism and to integrate the different compartments involved in lipid synthesis, storage and mobilisation (peroxisomes, lipid bodies, endoplasmic reticulum).

Yarrowia lipolytica belongs to the category of oleaginous yeasts, *i.e.*, yeasts able to accumulate more than 25% dry weight in lipids. *Y. lipolytica* is the only oleaginous yeast, for which Xomic and Molecular Biology tools are available, able to utilise efficiently hydrophobic substrates with potential applications in the green chemistry (biofuel and oleochemistry). This is why we choose this yeast a model for the systemic analysis of lipid metabolism.

During the last four years, team works were presented in 26 publications and three patents revealing the team dynamism.

Team : Expression and secretion of proteins

The committee expressed some concerns with regard to the future projects that have been presented. These projects will lead to invest the field of microbial ecology. This evolution is due to recent progresses gained in the understanding of the microbial communities involved in cheese ripening. They include yeasts and bacterial species and reduced ecosystems have been defined composed of a reduced number of strains whose genomes are now decoded. These "gnotobiotic" cheeses open the opportunity to study the dynamics of these ecosystems at the molecular level using X-omics methods. Moreover, we have the know-how and the molecular biology tools to handle two of the main yeast partners *Yarrowia lipolytica* and *Kluyveromyces lactis*. We see large opportunities to make important contributions in this field of research. Our current work on sulfur flavour biogenesis is only a first approach to these ecosystems. This project will take advantage of our integration in the MICALIS scientific project.

MICALIS

The committee expressed some concerns about the integration of some of our research projects in the MICALIS scientific project. So we would like to mention that even though the major structuration features of the future Micalis Unit were already defined when the evaluation took place, the detailed project was still under construction. The MGM scientists have more recently been heavily involved in the discussions about the Micalis project that allowed them to show how their projects will complement other ones carried out by other groups and strengthen the overall Micalis project. For instance, it is clear now that the different yeast research groups will widen the scope of the Micalis project and strengthen each of the three departments of the future Unit. Obviously, the MGM scientists will also gain access to more research platforms and to modern research facilities. The integration in the same Unit will facilitate the sharing of technologies, methodologies, and biological questions between different groups and compensate for the limited size of some of these groups. Therefore, we are convinced that Micalis brings more opportunities than threats for MGM scientists.

