

Génétique microbienne

Rapport Hcéres

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

Section des Unités de recherche

Evaluation Report

Research unit

Microbial Genetics Unit - INRA 0895

National Institute for Agricultural
Research



April 2009



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Section des Unités de recherche

Evaluation report

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National Institute for Agricultural
Research



Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

April 2009



Evaluation Report



The research unit :

Name of the research unit : Microbial Genetics Unit

Requested label : Unité INRA

N° in case of renewal : 0895

Head of the research unit : M. Philippe NOIROT (ex M. Stanislav EHRlich)

Research organization :

INRA

Date of the visit :

4 December 2008



Members of the visiting committee

Chairman of the committee :

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

Other committee members :

M. Bernard DUJON, Institut Pasteur, Paris, France

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

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

Ms. Carol MUNRO, University of Aberdeen, United Kingdom

M. Vincent MARECHAL, Université Paris 6, France

INRA representative :

M. Christian BOUCHER, Toulouse

Observers

AERES scientific representative:

M. Stéphane MERESSE

INRA representative :

M. Stéphane AYMERICH, Jouy-en-Josas



Evaluation Report



1 • Short presentation of the research unit

- Number of lab members : 59 including
 - 21 researchers including 20 from INRA and 1 from CNRS
 - 9 postdoctoral fellows
 - 12 PhD students, all with a fellowship
 - 17 engineers, technicians and administrative assistants
- Number of HDR : 10
- Number of students who have obtained their PhD since 4 years : 11
- Number of lab members who have been granted a PEDR : 0
- Number of “publishing” lab members : 18

2 • Preparation and execution of the visit

All members of the visiting committee received the well-prepared activity report and associated scientific project well on time to allow appropriate preparation of the visit. The committee appreciated the quality of the organization of the visit.

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

Over the past 4 years, the Microbial Genetic Unit moved from molecular biology of lactic acid bacteria relevant to the dairy industry to the study of the interactions of the human gut microbiota with its host. This transition from one field of expertise to another required both a strong scientific leadership as well as significant efforts from all teams that composed the unit. The overall excellent quality of the work produced, the involvement of the unit in ambitious national and international programs as well as the recognized capacity of future Head of unit to take over and continue to implement the scientific transition should contribute to the further success of the unit.

4 • Specific appreciation team by team

Team : Food bacteria and commensal

The scientific activities of the team « Food bacteria and commensal » recently underwent a transition, switching from the study of gene regulation in lactic acid bacteria to the study of commensal / host



relationships. The committee appreciated the efforts of the team that had to leave a field in which they were very productive, with a very good level of publications (13 articles, 10 directly led by the team, including 5 J. bacteriol, 1 Mol. Microbiol), to produce the groundwork on the commensal *Streptococcus salivarius* as a new model for functional studies.

Capitalizing on its strong experience on *Lactococcus lactis* and *Streptococcus thermophilus* molecular biology, the objective of the team is to produce fundamental knowledge on the molecular mechanisms of microbial adaptation within complex mucosal flora. For this, the team performed comparative genomics focusing on the understanding of the population structure of *S. salivarius* and *S. thermophilus*. They also chose to focus on a few potential adaptative phenotypes such as *S. thermophilus* exopolysaccharide production or *S. salivarius* immuno-modulatory functions.

Despite the quality of the team and its potential for collaborations in MICALIS, the presented projects were perceived as still too open and it was not completely clear to the committee what the scientific priorities of the team will be in the very near future. Moreover, although the team's evolution corresponds to the new orientation of INRA research towards health and nutrition, the committee expressed concerns about how good a model *S. salivarius* will fit to perform the projected functional studies.

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	B

Team : Adaptation of firmicutes to their environment

The team investigating the "Adaptation of firmicutes to their environment" was recognized as performing research of an excellent standard. Over the last two years the team has shifted focus from lactic acid bacteria of importance to the dairy industry in order to study the interactions of the human gut microbiota with the host. This transition appears to be progressing smoothly with the team applying their expertise to a wider group of organisms. The group has a strong publication record (14 articles in good journals of the field, including 5 proteomics, 1 PNAS) and has developed key collaborations with industry and with international research groups (including acting as co-ordinator). The team has taken on board novel and innovative bioinformatics approaches to identify surface exposed proteins of Gram-positive bacteria. The research question and objectives are clearly defined with achievable goals. The experimental pipeline will culminate in heterologous expression of surface exposed proteins that will be screened for properties that are relevant to understand their roles in interactions with the host. Some of these screens have already been applied to a number of different bacterial species, and isolates of the same species, and have showed the different bacteria elicit different levels of anti-inflammatory response. On the whole the committee was highly impressed with the research project. One minor concern was that the immuno-stimulation assay would only provide a partial picture of the ability of surface-exposed bacterial proteins to elicit host immune responses. Therefore, the committee would encourage this immunological-based screen to be widened. In addition, it was apparent to the committee that these approaches would have added value if coupled with gnotobiotic and knock out mouse models to examine host-microbiota interactions.



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A+	A+	A+	A+	A+

Team : Analysis of bacterial genome

The committee appreciated the good scientific production of the team "Analysis of bacterial genomes" for the last four years (10 articles in collaboration including 4 as major contributors). It was evident that an important part of the team's productivity results from collaborative projects with other teams from the unit or with a team called to join MICALIS in the future. This illustrates the importance for the unit of this team's knowledge and expertise in DNA sequencing, annotation of genomes, and general analysis of the data. As anticipated by the group, this role is bound to become even more important in the future, considering the development of the new high-throughput sequencing technologies and in the context of the development of metagenomic and system biology programs in the unit. Recent efforts made by the team to make these strategic new technologies available to the community were therefore highly appreciated. Concerning future research projects, the committee was more critical since, beyond the purely descriptive aspects of the proposed project, the scientific questions to be addressed were not clearly perceived. Therefore the team is strongly encouraged to prioritize and to focus on defined scientific objectives, taking into account the presence of a young researcher in this group who will have to develop a personnel project in the future.

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B	A	B	B	B

Team : Replication and central carbon metabolism

This team has long been involved in the analysis of DNA replication in *Bacillus subtilis*. Notably, it contributed to demonstrate the *E. coli* and *B. subtilis* replication machineries were different both in composition and activity. For the past 4 years these investigations led to only a few publications however of excellent level (5 publications, 3 as leading author, including 1 J. Biol Chem and 1 PLoS ONE). Mainly, the project that was presented is based on the recent discovery that an intimate interplay exists between the central carbon metabolism - and more especially the bottom part of glycolysis - and several enzymes of the replication machinery in *B. subtilis*. This discovery can be considered as a major advance in the field and should therefore be regarded as a starting point for essential investigations concerning replication-metabolism relationships. The scientific proposals are clearly defined. The investigations will rely on potential national and international collaborations. However, the committee has some concerns regarding the small size of the team and the lack of non-recurrent funding for the past several years, which may be a



serious limit in achieving this very ambitious project. The committee therefore suggests identifying solutions to strengthen this team.

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A	A	B	A	A+

Team : Functional integration of cellular processes in bacteria

The team activities have been mainly centered on the use of network interaction analysis to study different cellular processes in *Bacillus subtilis*. The group has an important publication record in highly recognized journals (23 publications, 12 as leading authors, including 1 Mol. Microbiol, 1 Dev. Cell, 1 Embo J. 1 PNAS). Interactions with teams devoted to mathematical modeling were seen as of important and valuable asset, necessary for the future development of research within the umbrella of systems biology. Another important research area has been the functional analysis of protein multi-complexes in order to determine the amino acid residues implicated in the interaction of the different components of the complex. This study, besides its intrinsic interest, had the long-term goal of developing algorithms that could predict the interactions when faced with unknown protein complexes. The committee felt that although the idea is of great value, this goal could be difficult to achieve due to the peculiarities of each protein structure. The project line dedicated to cell morphogenesis (Cytoskeleton and cell shape determination) presented very interesting results with high potential. However, this project was not perceived as directly related to the main interests of the team, the committee therefore encourages a better integration of this project to preserve the scientific coherency of the team as a whole. As a general comment, the committee estimated that this group comes across as a well-established team with clear ideas for the future.

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A+	A+	A+	A+	A

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

The overall excellent quality of the work produced, the involvement of the unit in ambitious national and international programs as well as the recognized capacity of the future Head of unit to take over and continue to implement the scientific transition should contribute to the further success of the unit.



6 • Recommendations and advice

– Strong points :

Good publication record, strong scientific leadership.

Excellent level of participation in national and international funding programs.

– Weak points :

Relative lack of communication between the teams.

Perceived lack of downstream flow of information regarding the creation of the future Unit MICALIS.

– Recommendations :

As judged by the projects that were presented, the activity and expertise of the unit will likely be at the heart of the future MICALIS department. The committee therefore encourages the future Director of unit to develop or reactivate collective communication instances such as the mandatory Laboratory Board to better inform and prepare all unit's members about all aspects of the creation of MICALIS, the success of which will likely rely on the ability of all merging units to embrace a true culture of collaboration.

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A	A	A	A	A

Jouy en Josas, 3 June 2009

Subject: Comments from the Microbial Genetics research unit on the AERES evaluation report

To whom it may concern,

We are grateful to the scientific committee for the generally very positive evaluation of the work performed in the unit. However, we feel that the overall appreciation reflects only partially the activities of our research unit. The committee pointed out the major transition in the research themes that was undertaken from “molecular biology of lactic acid bacteria relevant to the dairy industry to the study of the interactions of the human gut microbiota with its host”. However, the committee did not seem to appreciate the scope and importance of the metagenomics effort undertaken to characterize the human gut microbiota, its synergy with the above transition, and its integration in the projects of three teams. In this context, the project of the team “Analysis of the bacterial genome” represents an important technological challenge, and we cannot agree with its qualification as “purely descriptive”.

Similarly, we feel that the overall appreciation does not reflect the scope of the systems biology effort initiated in 2006 and pursued in our research unit. This represents another major transition from molecular biology of individual processes to systems biology, which was undertaken in close collaboration with mathematicians and bioinformaticians.

We are convinced that the brevity of the review (1 day) combined with a very rigid agenda of the visit (e.g. 30 min presentation per team independently of the size and organization of the team), and with changes in the agenda imposed upon us the morning of the review (e.g. last minute cancellation of the meeting between the new director and the review committee) did not facilitate in-depth discussions with the review committee.

Sincerely,

On behalf of the team leaders, and project leaders of the Microbial Genetics unit

Philippe Noirot
Director of the Microbial Genetics research unit

