LCB - Laboratoire de chimie bactérienne

Rapport Hcéres

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

Section des Unités de recherche

AERES report on the research unit

Laboratoire de Chimie Bactérienne

From the

CNRS

Université de la Méditerranée

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Le Président de l'AERES

Didier Houssin

Section des unités de recherche

Le Directeur

Pierre Glorieux

February 2011

Research Unit

Name of the research unit: Laboratoire de Chimie Bactérienne

Requested label: UPR

N° in the case of renewal: UPR-CNRS 9043

Name of the director: M. Frédéric BARRAS

Members of the review committee

Committee chairman:

M. Germain TRUGNAN, Université Pierre et Marie Curie, Paris

Other committee members:

M. Olivier POCH, Université de Strasbourg, Strasbourg, France

M. Serge POTIER, Université de Strasbourg, France

M. Fabrice RAPPAPORT, Université Pierre et Marie Curie, Paris, France

M. Hendrik VAN VEEN, Cambridge University, Cambridge, UK

Ms. Cécile WANDERSMAN, Institut Pasteur, Paris, France

Ms. Bénédicte MICHEL, Gif-sur Yvette, CoNRS representative

Observers

AERES scientific advisor:

M. Gérard CORTHIER

University, School and Research Organization representatives

M. Pierre CHIAPPETTA, Université de la Méditerranée

M. Jacques MARVALDI, Université de Provence

Ms. Martine DEFAIS, CNRS

Report

1 • Introduction

- **Date and execution of the visit**

The site visit has been organized from February 7 to 9, 2011. The scientific program included an overall presentation of the Unit by its Director followed by 14 scientific presentations of the past activity and projects by the team leaders. Two additional presentations were devoted to the description of the two internal platforms. Meetings with PhD students, engineers, technicians and administrative staff, researchers with permanent positions were also organized.

- **History and geographical localization of the research unit, and brief presentation of its field and scientific activities**

This unit has been an UPR CNRS since 1964 and there is now an agreement between CNRS and Université de la Méditerranée. The Université de Provence also contributes to this Unit.

The LCB occupies 1380 m2 on the Joseph Aiguier campus in Marseille, namely in buildings B, B' and IM. Part of these labs are under rehabilitation since 2008 (end of rehabilitation expected in 2011), with several teams having to move.

The LCB is dedicated to the molecular analysis of bacterial physiology. A large diversity of bacterial types are studied using a vast range of approaches: microbiology, molecular biology, biochemistry, structural biology, genetics, bioinformatics and cell biology. Most of the topics developped in the LCB focused on five central themes: energetic metabolism, metalloprotein biogenesis, stress response, signal transduction and regulation, cellular morphogenesis and motility. The unit is composed of 14 teams of very different sizes (ranging from 1 to 8 permanent people). Each team is focused on a specific topic and propose several individual projects. Two methodological platforms, namely "biosensors" and "biophotonics" have been implemented and collaborate with most of the LCB teams and outside within IMM (Institut de Microbiologie de la Méditerranée), a federative structure.

- **Management team**

The LCB is headed by M. Frederic BARRAS. The Unit has a laboratory council that includes 6 researchers, 4 ITA and 1 student. This council meets 4 times a year. All group leaders meet monthly.

- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	14	14
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	18	19
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	11	7
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	22	23
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	9	6
N6: Number of Ph.D. students (Form 2.7 of the application file)	18	20
N7: Number of staff members with a HDR or a similar grade	19	17

2 • Overall appreciation on the research unit

- **Summary**

The LCB is a one of the French leading units in microbiology. The global scientific outcome of the lab is excellent. Scientific themes covered by the Unit have been well selected to match up-to-date questions in the field of microbiology that have general implications for modern biology. The overall scientific production is quite impressive (180 published papers within the evaluation period for 32 producing researchers, including highly ranked both general and specialized journals: EMBO J., PNAS, PLoS Biol, PLoS Genet., J. Biol. Chem., JACS, Mol. Microbiol., J. Bacteriol., Nat. Rev. Microbiol...), with however disparities between teams, few of them being weaker. The Unit is highly reactive both in term of recruitment of young researchers (+4 CR, 1PU, 5 MCF) and for funding opportunities (see below). The unit also actively explores novel ways to commercialize the scientific knowledge gained.

The proposed projects are mostly based on very original results previously obtained by the teams. Most of the bacterial species, the molecular tools, the technologies and the concepts are present within the Unit and are fruitfully shared between teams.

The overall opinion of the committee is highly favorable for the unit as a whole and for most of the teams. Some internal adaptation may be proposed to reinforce the strengths of each of the unit components. This unit must be strongly supported as one internationally visible French microbiology unit.

- **Strenghts and opportunities**

- There is a very clear strategy and a global coherent vision of modern microbiology research (themes, studied organisms).

- Large technological skills are available, daily use of multidisciplinarity (microbiology, biochemistry, chemistry, genetics, biophysics, cell biology and imaging, bioinformatics...).

- The Unit have a high vitality, active scientific life within the unit, recent recruitment of young researchers and engineers, with some “raising stars“ scientists.

- The Committee observes an originality of recent discoveries, with an excellent level of publication.

- Excellent management and experienced leader of the Unit.

- The Unit have an industrial attractivity with several grants and patents.

- The Unit have an international recognition of most of the team leaders and of the Unit director.

- Strong support is given from CNRS and Universities.

- There is an overall good funding strategy with numerous national and international grants.

- The Committee observes a strong attractivity for master, PhD students and post-doc.

- The Unit have a capacity to generate internal platform ("MetBioLabs") with high skills and good involvement of the unit and the teams in their functionning.

- **Weaknesses and threats**

- Few teams are too small and/or weak;

- Few researchers do not publish on a regular basis;

- Cell biology and structural biology may be considered as useful approaches for future developments;

- Some teams have no technical help;

- Lodging problems are not yet fully solved;

- Some researchers have very heavy teaching or administrative duties that have to be compensated by additional positions;

- The possibility to group teams within departments has been discussed but appears to be inadequate at that time. The committee agrees with this choice and considers that the unit and its director have enough capacities to manage transient difficulties that have already or may happens.

- **Production results:**

A1: Number of permanent researchers with teaching duties (recorded in N1) who are active in research	14
A2: Number of permanent researchers without teaching duties (recorded in N2) who are active in research	18
A3: Ratio of members who are active in research among staff members [(A1 + A2)/(N1 + N2)]	100
A4: Number of HDR granted during the past 4 years	6
A5: Number of PhD granted during the past 4 years	26

3 • Specific comments

• Appreciation on the results

The Unit as a whole and each of the 14 research teams cover a very large field within microbiology. Most of the projects deal with hot topics at the cuting edge of microbiological research. Several results have deep implications for the understanding of specific bacterial species. Most interestingly, the LCB has provided news results that help or will help to understand at the cellular and molecular level more general topics for living organisms, such as oxidative stress, FE/S centers, metal management in living organisms, organization of membrane proteins, energy metabolism and respiratory systems, cell biology of the cytoskeleton and motility, cell signalization, cell architecture, mecanisms of multicellular organisms formation, ecology and evolution.

During the evaluated term, the LCB published 180 papers. More than 60 publications were in journals with IF>5 (JBC, Mol. Mic., PLoS Genet., EMBO J., JMB, PNAS, PLoS Biol., JMB, and prestigious reviews such as Nat. Rev. Microbiol, Curr. Op. Microbiol.). The unit mainly published in microbiology journals and chemical biology journals with some papers in new aera including environmental microbiology, genetics and bioinformatics. Twenty six theses have been defended, all have been productive (1 to 5 papers by thesis).

Members of LCB have obtained several prestigious awards: 2 CNRS bronze medals, nomination as senior IUF member, Prix Jacques Monod, Integration grants Marie Curie, ATIP, ERC Junior. Five team leaders are member of editorial boards in renowned journals: J. Bact. Microbiol., AEM, JMMB, Frontiers Biosciences, BMC Microbiol.

The LCB researchers have been invited in more than 50 national and international meetings, including some very prestigious congresses.

During the past term, LCB has recruited 9 young researchers (3 CR, 4 MC) and a whole group (working on cellulosomes) arrived. In the meantime, 12 engineers and technicians have been recruited. Twenty PhD students and 7 post-doc are currently present at LCB.

The LCB members have been highly successful in fund raising with 13 ANR contracts (PI for 7 and partner for 6). Fundings have also be obtained from FRM, HFSP, PACA region and a junior ERC grant has been obtained for 2011. Funding from industry have also been obtained.

The LCB has developed a dense network of national and international collaborations, described in the detailed team-by-team section. Main international collaborations include: participation to EU networks, USA, UK, Germany, Venezuela, Chile, Japan and a special mention for China where several collaborations have been undertaken with researcher and students exchanges.

Five patents have been registered (3 world, 2 European). Industrial collaborations are covered by 6 contracts for an overall amount of > 1 M€.

• Appreciation on the management and life of the research unit

The mode of organization of the unit is described by all the members of the unit as very efficient. The Unit Director is recognized as highly competent and charismatic. His involvment in the unit life is exceptional. The LCB functions with a lab council with elected members (4 meetings per year), a group leader meeting (monthly) and general assembly when required. Scientific animation is based on weekly scientific meetings (The “LCB Thursdays“) Journal clubs and students journal clubs and participation to IFR (IMM) seminars. The LCB also organizes “l’école thématique de microbiologie“ that is a national recognized event.

Hygien and security and permanent formation for LCB members are efficiently taken into consideration.

The 14 researchers with teaching duties ensure full-time duties (192h/year) except for the Unit director (IUF senior member). They teach at L and M levels. Two of the team leader are responsible for Master mentions. One team leader is the dean of the Faculty of Sciences. In addition most of the full-time reseachers are invovled in master courses. Members of the LCB also contributes to external communication activities (“Tous Chercheurs“, communication campain of RATP...).

- **Appreciation on the scientific strategy and the project**

Bacteria occupy a central place for the understanding of the diversity and the functionning of living organisms. Classical and unexpected functions have been developped by diverse bacteria, whose mechanisms have to be studied in-deep both for a better knowledge of the bacterial world but also for the living in general. Central functions in all the branch of living: breath, move, transform, adapt to or defend against environment, signal are recapitulated by bacteria and therefore bacteria represent a unique living laboratory.

LCB represent an excellent opportunity to develop concerted research projects that fulfill these general goals. Presence of most of the techniques, lot of species, huge knowledge ensure that substantial progresses will be made during the next term. This represents a true richness for french microbiology research.

Most of the proposed projects are in line with this global vision. Most of them are feasible, since knowledge, creativity, techniques and money are already present.

It should be useful to make this existing global strategy more visible and to reinforce some weaker groups by developing internal collaborations with stronger teams and by encouraging integrated strategies between themes.

Multiple tools both classical and innovative have been developed within the LCB. The decision to create two internal platforms, namely a new and original imaging facility core and a “biosensors lab“ is an excellent one. Both “MetBioLabs“ have started to produce interesting data and to collect grants that will ensure their autonomous functionning.

The excellence of the Unit project has been recognized by the fact that several cutting edge projects have been recently funded by ERC, HFSP, ANR.

4 • Appreciation team by team

- **Title of the team: Phage cycle and bacterial metabolism**
- **Name of the team leader: Ms. Mireille ANSALDI**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
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)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	2
N7: Number of staff members with a HDR or a similar grade	1	1

- **Appreciation on the results**

The group started in 2007. This recent team of modest size (4 people at the time of the visit, the team leader CNRS scientist, one technician, 2 PhD students) is interested in the control of temperate prophage lysogeny, and in the reasons for the presence of a relatively high proportion of DNA of phage origin in bacterial genomes.

The group has published 6 papers since 2006, including 4 as first or co-author (Mol Mic, JBC) and two as last author in 2010, one in Virology and one in a specialized journal of higher impact factor (9.5) Plos Genetics. The PhD student who is first author on these two papers obtained his PhD in 2010.

There are stable and productive collaborations with other groups in the unit, and outside the Unit with labs in Toulouse and Georgia. The group actively participate to the Consortium Biosensor (several academic partner and a private one).

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

The group has enroled two PhD students during the considered period, including one in co-direction with a researcher in Georgia (USA).

Several grants have been obtained: 2008-2012 ANR « blanche» (302 kE). 2005-09 ANR « Jeunes chercheurs » (150 kE). Région PACA 2009-10 (25kE) Prog CNRS 2009-10 (25 kE).

The group has a very good scientific visibility with 14 participations to meetings, including 6 international and 8 national meetings.

The group is involved in teaching in License and Master degrees. The team leader is co-organiser of the “Ecole thématique de Microbiologie”, a renowned national initiative. The team leader is also member of scientific Council of CNRS.

- **Appreciation on the scientific strategy and the project**

The group projects are mainly centred on the study of the genetic relationships between host general regulatory factors (chaperon proteins, transcription terminator) and prophage maintenance and/or activation, which are questions of general interest.

- **Conclusion:**

  - Summary

This young team, created in January 2007, is promising and very active. It compensates its small size by national and international collaborations. This is a very good team.

  - Strengths and opportunities

The dynamic young leader has been able to address and answer a variety of questions, which are fundamental (molecular genetic, bioinformatics) or applied (Biosensor), using temperate phages. Most of the projects are funded.

  - Weaknesses and threats

This is a small group that will need to reinforce during the next period.

- **Title of the team : Stress Adaptation in Enterobacteriae**
- **Name of the team leader : M. Frédéric BARRAS**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	2	2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	3	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	2
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		1
N6: Number of Ph.D. students (Form 2.7 of the application file)	4	3
N7: Number of staff members with a HDR or a similar grade	2	2

- **Appreciation on the results**

This team is an international leading group on Fe/S cluster biogenesis in bacteria with 14 publications during the last 4 years, all publications with members of the lab as last authors in highly rated journals: PNAS, JBC, Mol. Mic, Plos Genetics. In addition the team published one review in Nature Rev. Microbiol. and one text book chapter in the reference book *Escherichia coli* and *Salmonella*. The results and the production are of excellent level.

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

The group participates to international meeting: oral communications of several researchers from the lab (team leader invited at ASM 2007, Fe/S meeting in Athens 2009). Several seminars have been given in international Universities (NIH Bethesda, Berlin, Institut Pasteur, MRC London, Cambridge etc).

The group leader has been in charge of the organization of national and international congresses in France.

The team works in close collaboration with a lab in Grenoble for biochemistry and biophysics of FE/S clusters. This is a fruitful collaboration with several common publications.

The team has several PhD, M1 and M2 students. During the 4 years 4 theses were defended. The team contains two teachers-researchers (one PU one MCU) at "Université de la Méditerranée". The team leader has just been nominated as senior member of the IUF.

The team has good funding with 3 ANR (2 ANR "Blancs" and 1 MIE).

Together these performances provide an excellent visibility to the group.

- **Appreciation on the scientific strategy and the project**

The project for the next years comprizes the study of new components of the Fe/S biogenesis and delivery, the understanding of the stress resistance of the Suf system, the regulation of Isc and Suf. The team develops a new project which deals with various stress resistance mechanisms of Salmonella typhimurium in the phagosome. This is done in collaboration with a cell biology team in Luminy.

- **Conclusion:**

  - Summary

This is an excellent team. The group is working for many years on Fe/S biogenesis in bacteria mostly in E. coli and Erwinia chrysanthemi. They have done major breakthroughts in the field by genetic approaches and also by biochemical studies performed in collaboration. They have performed conditional lethality studies of various combination of iron sulfur synthesis mutants and discovered new intervening proteins and major interactions and regulations of the 3 major pathways.

The isc Iron sulfur cluster is more sensitive to oxygen radicals, the more resistant system Suf is induced during oxydative stress . Thus the group started to study the mechanisms of Fe/S regeneration and the bacterial defense against oxydative, acidic and metal stress. These new projects are also very competitive and already gave several excellent publications.

  - Strengths and opportunities

There are important breakthroughts in their field internationally known in the field of Fe/S clusters with reviews in Nature and major text books. The team starts on new cell biology thematic and has any national collaborations.

  - Weaknesses and threats

The team should find new post docs.

The team should go to international congress, start collaborations to recrute american post docs.

- **Title of the team : Genetic studies of the energetic metabolism of Acidithiobacillus Ferrooxidans and Thiomonas sp.**

- **Name of the team leader: Violaine BONNEFOY**

- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
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)	2	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	
N7: Number of staff members with a HDR or a similar grade	1	1

- **Appreciation on the results**

The team aims at understanding how *Acidithiobacillus ferrooxidans* and *Thiomonas arsenitoxydans* deal with toxic acidic and heavily loaded in metal/metalloids environments, focusing on the oxidation of ferrous iron Fe(II) and reduced inorganic sulfur compounds, RISC by At. f*erroxidans* and of *arsenite* (As(III)) by T. *arsenitoxydans*.

Concerning At. *ferroxidans* the team has provided (i) Demonstration that distinct strains exist and that they differ notably in the gene sets involved in Fe(II) oxidation pathways. (ii) Better characterization of the gene sets involved in the Fe(II) and RISC pathways and Fe(II) induced operons.

Concerning T. *arsenitoxydans*, the group has participated in the characterization of this new bacterial species to the complete annotation of the genes involved in the energetic metabolism and in adaptation to low pH.

Scientific production is very good considering the relatively small size of the group. The team leader has signed 11 original research articles (2 *PloS Genetics*) including 5 as last author (*Environ. Microbiol*, *BMC Genomics*). Other members of the team particularly the 2 PhD students supervised by the team leader are co- authors.

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

The overall appreciation is very good. The team leader has been invited as speaker in 3 international conferences and is a member of the editorial board of *Applied Environmental Microbiology*.

Many international collaborations have been established and the team is member of GDR CNRS « Métabolisme de l'arsenic chez les procaryotes : de la résistance à la détoxication ».

Projects have been well supported by numerous international (ECOS/CONYCIT Santiago, Chile; Biosigma, Santiago, Chile; 6th european PCRD) and national (ACI, ADEME) grants.

- **Appreciation on the scientific strategy and the project**

Most of the projects proposed are in collaboration within networks already established. Therefore they appear relevant and feasable despite the relatively small size of the group. The first one concerns energetic metabolism of

the iron oxidising *Acidithiobacillius ferrooxidans*. The goal is to test the putative role of RegA in the Fe(II) and RISC oxydation pathways and to determine the genes involved in growth of the bacteria under anaerobic conditions by comparison with growth in aerobic conditions. The second adresses the question of biofilm formation which is quorum sensing dependent (PICS CNRS network). Eventually, specific regulators of the aox arsenite oxydase operon of Thiomonas arsenitoxydans will be studied within the GDR CNRS « Métabolisme de l'arsenic chez les procaryotes : de la résistance à la détoxication ».

- **Conclusion:**

  - Summary

The scientific production of this group and its impact in the field of environmental microbiology are very good. The leader has an expertise in *Acidithiobacillus ferrooxidans* and more generally in iron and arsenic oxidation. One should nevertheless take care of the relatively small size of the group (the leader and a technician) and the current lack of financial support.

  - Strengths and opportunities

There is a good expertise of the team leader. Projects are supported by strong local, national and international collaborations.

  - Weaknesses and threats

Team well funded up to 2008 but no additional financial support for the next projects. Experiments on the bacteria studied much more fastidious than those on classical model bacteria (slow growth, poor cell yield, DNA transfer).

It might be necessary to make choices within the different projects (depending on the possibility of fundings) and to maintain the current collaborations. A recruiting of a post-doctoral or a PhD student would significantly help the group in carrying out its objectives.

- **Title of the team : Bacterial viability and oxydative stress**
- **Name of the team leader : S. DUKAN**
- **Staff members**

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

- **Appreciation on the results**

This group is interested in a phenomenon known for more than 20 years but only partly understood the phenomenon of Viable But Non Cultivable bacteria (VBNC). Decades of work have shown that oxidative stress needs to be overcome for growth restart of viable cells, and that a defect in oxidative stress defence can be at the origin of a VBNC phenotype. The laboratory has shown that protein oxidation, which leads to aggregation, is indeed an important component of the VBNC state. Protein carbonylation has been more particularly characterized.

The production is of very good quality since the team has produced a total of 12 publications in the past 4 years, including in Mol. Mic., J. Bacteriol and Plos One. Four PhD students obtained their PhD during the 4 years period. All but one signed at least two publications.

- **Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partners.**

The group has lost an active and talented scientist but has attracted a new post-doctoral fellow. Several financial supports from private origin were obtained during the period, for studies of VBNC on pathogenic bacteria (*Pseudomonas Aeruginosa* and *Legionella pneumophila*). One private support is still ongoing since a private company finances the present post-doctoral fellow.

- **Appreciation on the scientific strategy and the project**

The first project proposes the use of microfluidic chambers to study the expression of genes involved in cell defence against oxidative stress during growth restart from stationary phase, using measures of fluorescence to determine expression levels. The second project is a continuation of a previous work on the role of CO2 during oxidative stress, using transcriptional analysis. Both projects are feasible, although their source of financing is unclear at present.

- **Conclusion:**
  - Summary

The team has a good production in the past four years, but the group is presently fragilised by its small size (three people).

— Strengths and opportunities

So far, the group has demonstrated a good productivity and the projects on carbonylation and on the role of CO2 are original and promising.

— Weaknesses and threats

The future team of only three people seems quite small for all the proposed projects. Priorities should be defined to avoid dispersion of these limited forces.

The team leader should be careful of focusing more his research, given the new perimeter of the group.

- **Title of the team : Bacillus Subtilis ABC transporters: functioning and regulation**
- **Name of the team leader : Marilyne FOGLINO**
- **Staff members**

	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	0
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)		
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.7 of the application file)	4	1
N7: Number of staff members with a HDR or a similar grade	1	

- **Appreciation on the results**

The current and proposed projects for this team are very good. The group focuses on interesting and original lines of research on ATP binding cassette transporters in *Bacillus subtilis*. In particular, the group studies (i) the role of the *Mta* regulator in expression of 2 drug efflux pumps and a siderophore extrusion system, and (ii) the function of the ABC transporter BceAB and sensing two-component regulatory system (BceSR) in bacitracin resistance. By analysing global protein changes in a Δmta mutant, the group found a decrease in phosphorylation of CpgA a GTPase. Interestingly, in studies on revertants of the Δmta phenotype, a secondary mutation was discovered in prpC, the signal transduction phosphatase that dephosphrylates CpgA. The prpC-prkC-cpgA operon is well studied by different groups and was shown to be involved in biofilm formation, in sporulation and in sensitivity to antibiotics targeting peptidoglycan. PrkC has been shown to bind muropeptides. Thus, the main aim of the project is to understand the novel link between Mta and the prpC operon. The second project concerns the mechanism of bacitracin efflux in *B. subtilis*. The group discovered that bacitracin resistance is regulated by four proteins components, which form a histidine kinase sensor (BceS), a response regulator (BceR) and an ABC transporter (BceAB). The latter is required for induction of the operon and for bacitracin resistance. The extra cellular loop of BceB is required for resistance and induction. The project for the next years is to test other systems related to BceRSAB in *B. subtilis* and other firmicutes and to characterise the interactions between the four components.

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

The scientific output of the team is good. They have published 5 peer-reviewed papers in the past period in journals including J. Bacteriol., Plos One, J. Mol. Microbiol. Biotech. In addition, 4 PhD students and 3 Master students have completed their studies in this time, and have produced very good dissertations. The group needs further recruitment of postdoctoral fellows. The group has established good collaborations, in particular at the national level. The PI is invited to national meetings.

- **Appreciation on the scientific strategy and the project**

The group is funded by two ANR blanc grants, one on each of the two major lines of work in the lab. From the information provided it is not clear when the present funding will end, or whether new grant proposals have been submitted.

- **Conclusion:**

— Summary

The group has very good research projects, especially on the Mta regulation of the prpC operon, and this gives the group a unique position in the field. The publication output and impact of the research are good.

— Strengths and opportunities

In view of the fair number of Master and PhD students, a window of opportunity might be present to increase the number of research seminars and publications and their impact.

— Weaknesses and threats

The current group size and composition will impose limits on the number of topics that can be studied in parallel, and might make it difficult for the group to work on multiple competitive projects.

It would be advisable to focus research and to strengthen the research interactions with the teams in Paris Sud and Pasteur, which would support future activities on the link between Mta and the prpC operon.

- **Title of the team: Metabolism and regulation of cellular processes in B. Subtilis.**
- **Name of the team leader : A. GALINIER**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	3	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)		
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	1
N7: Number of staff members with a HDR or a similar grade	2	2

- **Appreciation on the results**

The overall assessment of the results of this team is very good. The team is mainly involved in original studies aimed at defining new relationships between bacterial carbon metabolism and cell functions. To this end two main axes have been developed: (i) to find out functional partners of Hpr, a phosphotransferase involved in carbohydrate uptake. Interactions have been found with GapA, a B. subtilis G3PDH. (ii) to search for proteins of unknown functions whose genes were found in the vicinity of genes involved in the carbon metabolism. The team discovered that YvcJ, a P-loop containing protein was involved in B. subtilis competency and that YvcK was related to MreB and thus to cell cytoskeleton. The team published 6 papers and a review during the last period, 2 of which in J. Bact. being directly the results of the team and the 3 others were in collaboration. There is a good participation to national and international meetings.

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

The visibility of this team is very good. The team is well integrated within LCB with several internal collaborations.

The team has been able to recruit a young CR2 that arrived in 2010 and has a very good production record, with 7 publications since 2006 including 3 as 1st author in Mol. Mic., PLoS Genetics, and Proteins. This CR2 was recipient of a “Prix Jacques Monod” by Fondation de France in 2008. Two PhD students have been enrolled since 2006. Both have published at least one paper in very good journals.

The team leader is a Partner in an ANR contract (ANR blanche) and will participate to a Marie Curie IRG for the next period.

The team members participate to several teaching activities at the Master level.

- **Appreciation on the scientific strategy and the project**

The project is in line with the former research activity and consists in studies dealing with strategies developed to adapt bacterial cellular processes to nutrient availability. The team intends to characterize the functions of YvcK and its main interactions, especially those with MreB and PBP1. Another part of the project will be to characterize GluP, an intra-membrane serine protease involved in glucose utilization and export. The project is well dimensioned and the team possesses the knowledge and the tools to succeed. The overall assessment is that this is a very good the project.

- **Conclusion:**

— Summary

The group has defined an original topic and has produced new and promising data during the past period. The project is well designed and the arrival of a new young and dynamic researcher represent a huge opportunity to reinforce the team.

— Strengths and opportunities

The team has accumulated a very good knowledge on his topic. Collaborations have been engaged with renowned scientists at the national and international levels. The team has recently demonstrated an excellent attractivity with the recruitment of a new CR2 CNRS. The group is well inserted within the LCB.

— Weaknesses and threats

The team has to improve its ability to raise funds on its specific topics and has to take care to improve the number and the quality of publications. The team leader should consider the possibility to communicate more efficiently the results of the team in international meetings to improve its visibilty.

Given the size of the project, it should be advisable to focus on more adequately defined questions and to recruit more PhD students and/or post-doctoral fellows. The team should take care to improve its international visibility.

- **Title of the team : Metalloprotein biogenesis and anaerobic respiration in prokaryotes**
- **Name of the team leader : Axel MAGALON**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	2	2
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)	2	
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.7 of the application file)	6	2
N7: Number of staff members with a HDR or a similar grade	2	2

- **Appreciation on the results**

The team is producing excellent research. The team is interested in the biogenesis of metalloproteins in general with an emphasis on molybdoenzymes, which are involved in the carbon, nitrogen and sulphur cycles. They have identified NarJ as being a dedicated chaperone that orchestrates the cofactor insertion, the subunit assembly and the membrane-anchoring step during the assembly of the nitrate reductase NARGHI. The motif required for the recognition of the nascent protein by NARJ has been characterized at the molecular level. In addition, using site-directed spin labelling and EPR spectroscopy, they have shown the importance of the conformational flexibility of NARJ in the recognition process and its specificity. Importantly the comparison with other multimeric Molybdoenzymes points to this assembly sequence being a general feature of the enzymes belonging to this family (2 JBC, 1 Febs J). Among the structural properties shared with other membrane proteins the nitrate reductase binds a cardiolipin. The team members have shown that the role of this lipid is not only structural but that it is also essential for the function since its presence is required for the appropriate binding of the substrate. From a functional standpoint, the nitrate reductase has the rather rare ability to stabilize very efficiently a semiquinone radical. In collaboration with others, the team members have used state of the art EPR technics to characterize the structural determinants underlying this ability. They have shown that the nitrate reductase can stabilize with a similar efficiency, either a menasemiquinone or a ubisemiquinone, an expected observation owing to the very different midpoint potential of the menaquinone/menaquinol and ubiquinone/ubiquinol redox couples.

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

The quality and the number of the publications by the team are excellent. They have published 11 papers in peer-reviewed journals and 1 review (Coord Chem Rev). The team members appear as PI (1st or last author) in 7 out of these 11 papers: (1JACS, 1Febs J, 3 JBC, 1J PhysChem B, 1 Biochemistry). They have co-authored 1 paper in PNAS. Publication by PhD students is excellent. The team has established interactions in France with the “Groupe Francais de Bioénergétique” and “Club Métalloprotéines et Modèles”, and is also regularly invited for International meetings suggesting that stable interactions have been formed.

- **Appreciation on the scientific strategy and the project**

The team has an excellent record in fund raising: 1ANR JC and 1ANR PCV (as PI) and 1 ANR as partner. Presentations in two Gordon Conferences, and one international meeting in EU. PI is regularly an invited speaker National Universities and abroad. Invitations to Gordon Conferences suggests existence of very stable interactions with foreing partners. The team is composed of 3 permanent scientists (1 CR1 CNRS, 1 DR2 CNRS, 1 MCF) and 2 engineers (CNRS). In addition 6 Ph D students contributed or contribute to the projects led by the team, with an average of 3 PhD during the evaluated term. The team is attractive for new PhD students (6 students during the evaluated term), and is well funded, mainly through ANR. The team leader has excellent international recognition. He has been invited to 4 international conferences including 2 Gordon research Conference and has been awarded the CNRS Bronze medal in 2007. The objectives in the planned project for the next four years are in line with the previous research axis.

- **Conclusions**

  - Summary

Over the past years, the team has carried out excellent and innovative research on metalloprotein biogenesis and anaerobic respiration with excellent output in publications, awards, and excellent visibility in international meetings.

  - Strengths and opportunities

The excellent results obtained by the team are an impressive example of a fruitful multidisciplinary approach aimed at the understanding the biogenesis and function, at the molecular level, of an important enzyme. It is a demonstration of the importance of funding multidisciplinary research with strong and long-term collaborations.

Although the group might have to narrow their focus in the future, we recommend the group to continue with the promising and excellent work.

  - Weaknesses and threats

The possible reduction in the size of the team during the course of the next term, related to the retirement of some of its members, raises a minor question regarding continuity in expertise and know-how.

- **Title of the team : Biogenesis and regulation of anaerobic respiratory systems**
- **Name of the team leader : Vincent MEJEAN**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	2	2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	
N6: Number of Ph.D. students (Form 2.7 of the application file)	4	1
N7: Number of staff members with a HDR or a similar grade	1	

- **Appreciation on the results**

The team's main interest is the Trimethyl oxide reductase Tor system, which is found in many gram-negative bacteria such as *E. coli* or *Shewanella oneidensis*. The Tor system is made of a periplasmic terminal enzyme, which drives Trimethylamine oxide reduction. TorA is a molybdoenzyme and the team has shown that its biogenesis involves a chaperone, TorD, which is encoded by the last gene of the tor operon. By binding to the signal peptide of the apo TorA, Tor D protects it against proteolysis. Interestingly TorD also interacts which the last player in the cofactor synthesis pathway, MobA, so that it is proposed to act as a platform connecting the apoTorA and the cofactor delivering subunit MobA. Importantly, the comparison of the structure of TorD to that of functionally analogous chaperones points to a conserved fold allowing one to define a chaperone family involved in the biogenesis of many metallo proteins.

Whereas it was commonly accepted that the Tor system is only induced under anoxic conditions, the team has shown that it is not only expressed in the presence of oxygen but also functionally active. This is all the more surprising and important as E. coli bears various oxidases, among which bd oxidases which are characterized by an extremely high affinity for oxygen. Under aerobic conditions, the role of the Trimethyl oxide reductase pathway would thus rather be a redox valve than an indispensable bioenergetic chain.

In addition, the team has recently shown that the taxis toward TMAO requires an active Tor system. This suggests that the taxis requires TMAO to be metabolized so that it should be considered as an energy taxis rather than a chemotaxis properly speaking, thereby shedding a new light on this topic. The team has identified one the key actor in the energy transducing chain in Shewanella oneidensis. The team is composed by 1 DR, 1 CR, 1 assistant professor and 2 technicians (one having joined the group in 2010). 1 CR left the group in 2007.

During the evaluated term, 2 PhD (2004-2008) have defended their thesis.

The team has published 15 papers in peer-reviewed journals among which 9 are co-authored by team members as PI (1st or last author). 3 JBC, 2 Mol Microbiol, 1 Biochem Biophys Res Co, 2 FEMS Microbiol Lett. The publication record can thus be considered as very good.

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

As mentionned above the team is attractive in terms of its ability to gather young scientists. With 3 invitations to international meetings, the PI is undoubtedly internationaly recognized as being an expert of the TMAO system and the results recently obtained on the involvement of TMAO in aerobic conditions and in energy taxis significantly renew the vision one had on the subject.

The Team has also been successful in fund rising, 1 ANR (partner), 1 Programme Interdisciplinaire Energie CNRS (partner), 1 Contract Veolia/CNRS (PI), 1 PEPS and 1 Action Thématique as PI and is involved in international networks such as the one with a german group funded by the Procope program.

- **Appreciation on the scientific strategy and the project**

The projects are in line with the previous research axis: They include the continuation of the work on the biogenesis of the Tor system and aims at the identification of the full set of actors and at characterization of their interactions. The chemotaxis or energy taxis project is grounded by a series of original and important observations and will be pursued. This last new axis clearly deserves being pursued as it constitutes a remarkably original project which can potentially provide important insights into the integration of the aerobic function of the TMAO pathway and the cell motility.

- **Conclusion:**

— Summary

The team is recognized at the international level for its expertise in the biogenesis of the Tor system. Its scientific production in this field is very good and its recognized know-how warrants the success of the different approaches considered in the project. The Chemotaxis research line has been recently launched and is grounded by original observations made by the team. The main concern is the balance between the ambition and diversity of the projects and the size of the team. This could be secured by a more ambitious fund raising strategy, which, if successful, would allow the team to rely on 3-4 years contracts rather than the one-year contracts obtained recently.

— Strengths and opportunities

The international recognition and the team combined with the original observations made on energy taxis constitute remarkable grounds.

The scientific production of the team is very good and its recognized know-how warrants the success of the different approaches considered in the project. The Chemotaxis research line has been recently launched and is grounded by original observations made by the team. The main concern is the balance between the ambition and diversity of the projects and the size of the team. This could be secured by a more ambitious fund raising strategy which, if successful, would allow the team to rely on 3-4 years contracts rather than the one year contracts obtained recently.

— Weaknesses and threats

Mid-term to long-term funding would secure the project. The ambition and diversity of the projects, which are legitimate considering the know-how of the team, is not commensurate with the size of the team.

- **Title of the team : Cell biology of bacterial motility.**
- **Name of the team leader : Tam MIGNOT**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
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)	4	2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.7 of the application file)	3	1
N7: Number of staff members with a HDR or a similar grade	1	

- **Appreciation on the results**

This team is a very young team headed by a CR2-CNRS recruited in 2006. The team is working on a well-defined topic related to the molecular mechanisms of bacterial motility and more specifically on the A-engine, one of the two motility systems. The experimental strategy ingeniously combines genetic, cell biology, cell imaging and biophysical approaches. The team has demonstrated that the A-motility engine involves the bacterial actin cytoskeleton (MreB) and a ras-like G-protein (MglA) to position the focal adhesion complexes. In addition, a proton channel was shown to be involved in bacterial motility. The role of slime secretion has been studied using a biochemical approach. The team has also started to address the question of the regulation of the directionality of bacterial motility and to study the involvement of Frz and of small GTPases.

The scientific production is of high ranking: Science, Embo J., 2 Mol. Mic.(1 in collaboration), 2 J. Bact. (collaborations), 1 PLoS Biol., 2 PLoS One, among a total of 15 papers and 4 reviews.

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

The team leader has a very good international recognition with invitations in 5 international meetings (2 ASM, 2 STIM, 1 Gordon) since 2007. The team counts 4 post-doc 3 PhD students, and hosts M1 and M2 students. The team leader is teaching in the Master degree.

The team leader has received several important funding as PI including an ANR JC, a HFSP FRM, a Princeton University grant, and has recently obtained an ERC Young Investigator Starting Grant and a PACA grant obtained (2009) in collaboration with a local INSERM Unit.

- **Appreciation on the scientific strategy and the project**

The research project is in line with the team previous works and proposes to continue the characterization of the mechanism of A-motility, of the nature of the motility engine, and of the directional control of motility. This important work will have direct implications for bacterial physiology, pathogenicity as well as for collective movements of individual cells towards the formation of multicellular structures.

- **Conclusion:**

  - Summary

The team is studying cell motility using *Myxococcus xanthus* as a model. This bacterium has two types of motility Type IV and A-type motility. The group has unraveled the mechanisms involved in A motility and is trying to understand how the two types of motility are coordinated to allow movement in one direction. This involves a polar activity switch dependent on GTPases. In addition the group is studying the role of peptidoglycan and slime in this motility. The results have broad implications in cell movements in general.

This is an excellent young team, working on a fascinating and innovative area, using a combination of modern and potent approaches, which must be strongly supported.

  - Strengths and opportunities

It is a very good young team with excellent knowledge of the context.

The team has an excellent research network at local, regional and international levels and excellent funding opportunities

  - Weaknesses and threats

The team leader must rapidly defend his HDR (foreseen this year).

- **Tiltle of the team : Adaptative evolution of E. coli under pi starvation conditions**

- **Name of the team leader : P. MOREAU**

- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
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)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	0
N5: Number of 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)	1	0
N7: Number of staff members with a HDR or a similar grade	1	1

- **Appreciation on the results**

This team studies the survival of Pi starved cells in stationary phase. It is known that Pi starvation is lethal because of the production of oxidative damage. The results obtained have characterized the protection against Pi starvation by amino acids metabolism and has identified two genes involved in the phenomenon. Inactivation of rpoS or activation of the pseudogene phnE improves resistance to Pi starvation.

This work allowed the publication of two J. Bacteriol papers, one Mol Microbiol and one review. Two of these papers constitute the PhD thesis of a PhD student. Considering the very small size of the team, although modest qualitatively and quantitatively, the production is reasonable.

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

This very small team is composed of the team leader only at the time of the visit and has not specific source of financing. However, genetic experiments are cheap and can be financed with the recurrent credits.

The team leader actively participates to the life of the Unit.

- **Appreciation on the scientific strategy and the project**

This project proposes to pursue the characterisation of bacteria able to survive Pi starvation. It is original and interesting, however, it will remains modest since the team is now limited to one scientist.

- **Conclusion:**

  - Summary

A modest but stready production is observed, proportional to the size of the team. Since the team leader will retire during the duration of the next contract, the team will close and it would be counter-productive to precipitate the closure.

  - Strengths and opportunities

The team leader has a deep and broad knowledge of his field of interest.

  - Weaknesses and threats

Small size of the team is a weakness.

- **Title of the team : Genomics, Evolution and Bioinformatics**
- **Name of the team leader : Emmanuel TALLA**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	2	2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	0
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	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	2	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	3	2
N7: Number of staff members with a HDR or a similar grade	2	2

- **Appreciation on the results**

The team has been created in 2006 to bring bioinformatics expertise in the LCB unit. The team focuses on the genomics and evolutionary analysis of genome and proteome of organisms from the three domains of life, with a more pronounced interest for prokaryotic organisms. Through various external and internal collaborations, the team has provided major contributions in different axes of research among which it can be highlighted:

i) The annotation and proteome analysis of newly sequenced complete genomes encompassing fungi and bacteria.

ii) The definition of a minimal set of proteins to phylogenetically characterized the evolutionary status of Archaea. This has led to the characterization of a new archaeal group (*Thaumarchaeota*) allowing a better understanding of the complex evolutionary history of these organisms.

iii) The in depth in *silico analysis* (with various approaches encompassing annotation, comparative genomics, phylogeny…) of various biological systems involved in iron/sulphur cluster formation, RNA modification, aerobic respiration or cell division.

iv) The development of a specific biocomputing tools notably the CSPD (Carbonylated Site and Protein Detection) model, which invokes set of rules to better predict the Hot Spots of Carbonylation at the proteome level.

Over the past period, the team has published 29 publications in international journals, of which 12 originate from the team (first and/or last author) and 14 are in journals with the highest impact in the field. The overall publication record is good.

The group has developed a good network of collaboration both internally (10 publications with the other LCB teams) and externally (Genolevures consortium) in the framework of a complete teaching charge (192 hours/year for each PI).

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

The team has a good international visibility in conferences and is invited in 4 international conferences and various national conferences.

2 Master students (2008); 3 PhD defended, and one post-doctoral fellowship.

The team has successfully applied for competitive funding: 4 ANR as partner, 3 GENOSCOPE funding for sequencing and 1 ATIP grant. Currently, it is supported by 2 ANR grants.

The research is carried out within a network of collaborators with participation in 2 GDR CNRS and 1 Mobioloscope project.

- **Appreciation on the scientific strategy and the project**

The projects of the past will be extended and continued with established or new collaborations. The program exists for 4 years and is feasible if human support is available. Funding has been currently secured until 2012 via 2 ANR grants.

The continuation of the research program lacks originality. As mentioned, cutting edge approaches notably statistical tools are not available in the team and should be obtained locally or via collaborations, absence of such tools underpinned the problem of the actual and future deluge of genomic data which is not clearly addressed in the proposal.

- **Conclusion:**

  - Summary

The past, current and future research program is solid science that targets numerous aspects of genomics and phylogeny of living organisms. The record of the PIs may ensure results in the future.

  - Strengths and opportunities

The strength of the program is the experience of the PIs to work in the annotation and phylogenomics fields. This should also open up opportunities to uncover novel mechanisms and better understand the origin of numerous biological systems. The program can go beyond the annotation and description of the systems, notably via the strong integration of the results into the biological context provided by the unit teams. It would be advisable that the PI takes on the lead role in projects. Due to a lot of requests for collaboration, it will be required to do some choice.

  - Weaknesses and threats

A team with a very limited staff in view of the numerous and ambitious projects proposed in a very competitive field. The team might greatly profit of a more focused research area.

Most of the future research depends on collaborations and on annotation/analysis of biological systems with external tools; the investment and future efforts of the team in the development of the CSPD model (an original biocomputing development of the team) is not clearly delineated.

- **Title of the team : Cellulosomes and plant cell wall hydrolysis**
- **Name of the team leaders : Chantal TARDIF/ Henri-Pierre FIEROBE**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	4	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)	2	
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	5	
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	
N7: Number of staff members with a HDR or a similar grade	2	1

- **Appreciation on the results**

The group is currently studying production of cellulosomes enabling *Clostridium cellulolyticum* to degrade hemicelluloses and crystalline cellulose. The latter is the most abundant biopolymer on earth. The team is focused on functioning of cellulosomes and use of cellulosomes to engineer microorganisms of industrial interest.

During the last four years significative results have been obtained on plant cell wall degradation by *Clostridium cellulolyticum*. The team members have established the enzymatic diversity of cellulosomes by 2-D electrophoresis and by genomic and proteomic approaches. This diversity depends on an adaptation of the cellulosome composition to the substrate used. Among 63 putative cellulosomal proteins predicted by bioinformatics, only 30 were found in the 3 media tested. In addition, the team has studied the regulation of the genes encoding cellulosomal proteins (partly grouped in 2 clusters) and has set up genetic tools in *Clostridiae*, such as random mutagenesis to study the functions of cellulosomal enzymes in vivo. Specific adhesion of *Clostridium cellulolyticum* to cellulose fibers was highlighted and adhesion mutants were selected. Full length and artificial cellulosomes structures have been characterized. Artificial minicellulosomes engineered complexes composed of hybrid scaffolding containing two or three cohesin modules from divergent bacterial species and enzymes appended with the cognate dockerin modules have been used to dissect the mechanisms of action of natural cellulosomes. Eventually, using data obtained on natural and hybrid cellulosomes, the engineering of solventogenic industrial bacterium, industrial cellulase cocktails and industrial ethanol producers has been initiated.

The scientific production of the team is very good. During the last four years they have signed as first and last authors 10 publications in the best journals of microbiology (*1 J. Mol Biol, 1 J. Biol. Chem., 1 Proteomics, 3 J. Bact, 3 Appl. Environ. Microbiol*). Members of the team have signed five more collaborative articles. Two PhD students have been supervised and have defended their thesis with respectively one and three published articles as first author. Three among five submitted European patents applications have been published; the other two are still being examined.

Projects have been well supported by 2 ANR grants, a cooperation with « Total SA », a 6th/7th PCRD and Marie Curie Research Training Network.

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

The overall appreciation of these aspects is excellent. Team leaders have been invited as speakers in 3 international meetings. Three PhD students and a post-doc have been enrolled. Projects have been supported by 2 ANR grants, a cooperation with « Total SA », a 6th/7th PCRD and Marie Curie Research Training Network. The team is involved in international (University of Nottingham, UK: NREL, Boulder, Colorado; 11 partners of the Marie Curie network) and national (INSA, Toulouse) collaborations and in an efficient industrial partnership (Total SA, Paris).

- **Appreciation on the scientific strategy and the project**

The project is to study fundamental aspects of cellulolysis by *C. cellulolyticum*: identification of adhesion factors and adhesion/cellulolysis relationship, secretion and assembly of the cellulosomes, role of GH9 cellulases in the functioning of cellulosomes, regulation of cellulase and hemicellulase components. Putative industrial applications, such as the production of biofuel from biomass, will be explored by engineering a cellulosome in "*clostridio*" and by engineering a very interesting cellulolytic strain of *E. coli*.

The project for the next five-years is the continuation of the present works. The topics are original, the goals of the project are well defined and the project is supported by international and industrial grants. Expertise and skills within the group in cellular biology, biochemistry, genetics, microbiology are complemented by efficient collaborations with other groups of the Laboratoire de Chimie Bactérienne and by external collaborations. Achievements are expected in a better understanding of the cellulosome complexes, in the exploitation of basic data to improve cellulosome engineering, and in the transfer of engineered cellulosomes into industrial microorganisms.

- **Conclusion:**

— Summary

The team has an excellent expertise on cellulosome and its ability to degradate the cellulose, the limiting step of the carbon cycle on earth. It also has an excellent international visibility in the field attested by a very good scientific production during the last four years.

More generally, the team has the capacity to achieve many of the objectives proposed in the next project on cellulolysis by *C. cellulolyticum*.

A new team leader will be in charge of the next five-year project because of the retirement of the previous one at the end of 2011. During the past four-years this new team leader was in charge of many topics, he signed 3 publications as last author and supervised 2 PhD thesis. He is clearly able to efficiently drive the group.

— Strengths and opportunities

The team has a strong background on cellulosome, with an expertise in cellular biology, biochemistry and genetics approaches. The team is strengthened by the availability of proteomic, transcriptomic and microscopy platforms within or around the LCB. In other areas as biophysics collaborations have been established with national and international partners. Two european PhD fellowships were obtained for 2010-2013. The projects require technical staff to be successfully achieved. Replacement of the retired researcher (a PR1 professor at Université de Provence) must be considered as a priority in order to support the group.

— Weaknesses and threats

The only weakness is the lack of technical staff for the future project, taking into account that most of the researchers have important teaching duties and should be helped by a technician or an engineer. The threats generally depend on the ability to get grants and in particular the industrial partnership with Total SA appears to be necessary for achieving engineering industrial microorganisms.

- **Title of the team : Functional Architecture of Bacterial Cells**
- **Name of the team leader : Long-Fei WU**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	2	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	3	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	1
N6: Number of Ph.D. students (Form 2.7 of the application file)	3	2
N7: Number of staff members with a HDR or a similar grade	1	1

- **Appreciation on the results**

Taking advantage of a strong expertise in bacterial biology, the team has made a thematic switch towards the analysis of the genome and physiology of the magnetotactic bacteria (MTB). By isolating unknown MTB from the Mediterranean and China seas, defining laboratory growth conditions for these bacteria, and studying the original mechanisms linking flagellar apparatus and magnetosome, the team has become a world leader in the field. Notably, the understanding of the molecular links between the unusual flagellar apparatus and the MamK cytoskeleton allowed the team to propose a chemotaxis-like model for the locomotion direction of the MTB.

Over the 2006-2010 period, the team has published 30 publications in international journals of which 20 have a team member as first and/or last author and 10 are in journals with the highest impact in the field. Thus, the publication record is excellent.

Finally, it should be noted that the team has developed a very intense networking with China.

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

The team has a very good international visibility in conferences, invited in 3 international conferences. The team has a good attractivity with 1 Master student (2006), 3 PhD students, post-doctoral fellows, 2 Associated Researchers and 1 Professor hosted in the lab during the past period. The team is active in recruiting PhD students or post docs locally and from abroad.

The funding of the team is secured up to 2013. The team has succesfully applied for CNRS funding, for European and Human Frontier grants with the group leader as coordinator. The team was also supported by 5 ANR as partner and 3 GENOSCOPE funding for sequencing. Currently, it is supported by 2 CNRS grants and 1 CNRS-TOTAL contract.

- **Appreciation on the scientific strategy and the project**

The project is coherent, well structured and clearly feasible. The team proposes 4 research themes in continuation with the encouraging results obtained through the characterization of magnetotactic bacteria. After the determination and analysis of the complete genomes, proteomes and pathways of the studied magnetotactic bacteria,

the team intends to determine the assembly mechanism and 3D structure of the flagellar apparatus, the latter being done in collaboration with a structural team well-established in the field. A second project, which will be realized in collaboration with a NMR/Mass Spectrometry group, aims at understanding the molecular mechanisms involved in glycosylation of the flagellar apparatus. This will be done by developing original nanotechnologies in collaboration with experts in the field, and will aim at developing systems amenable to guide magnetotactic bacteria, which may have important biotechnological outcomes.

- **Conclusion:**

  - Summary

The team is of international excellence and addresses an original biological system poorly studied so far with a high scientific and technologic potential. In the immediate coming years the team is likely to maintain international relevance and excellence, although additional resources may be useful in the future to further develop the team adapt to changes in the field. Recruitment of at least a technician or an engineer is recommended and a politic to attract confirmed researcher is also recommended when considering the teaching duties of the team members and the intense networking with China.

  - Strengths and opportunities

The expertise of the team members in the biology of the magnetotactic bacteria is excellent.

The team has access to complementary expertise and technologies available in the unit.

The team has establishment of a good national and international collaborative network.

  - Weaknesses and threats

A team with a limited staff in view of the numerous and ambitious projects proposed in a competitive field.

- **Title of the team : Cellular differentiation and signallin**
- **Name of the team leader : CC. ZHANG**
- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	2	2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	4	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	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	6	1
N7: Number of staff members with a HDR or a similar grade	3	3

- **Appreciation on the results**

The focus of the team is the differentiation of heterocysts in the cyanobacterial model system Anabaena/Nostoc PCC 7120. These heterocysts, which are differentiated under nitrogen deprivation, express the nitrogen fixation pathway and in particular the nitrogenase, which is highly oxygen sensitive and must be protected from the oxygen rich compartment where oxygenic photosynthesis occur. Interestingly, the signal transduction chain that is activated under nitrogen deprivation is involved in the response to oxidative stress, which has led the team to extend its research topic to the signalling network activated under oxidative stress.

Heterocyst differentiation:

The results obtained by the team has allowed starting to disentangle the signalling pathway. 2-oxoglutarate has been indentified as being the triggerring signal. It binds to a transcription factor (NtcA) and this binding enhances the binding of the transcritpion factor to DNA. In addition, the team has identified one phosphatase which is involved in heterocyst differentiation and could contribute to the signalling network. A collaborative project has led to the determinaton of the structure of the NtcA receptor both in its apo and 2-oxoglutarate bound forms which has grounded a study of the structure/function relationships of this protein by a site directed mutagenesis approach.

Another issue, which need to be addressed, is the cross talk between Nitrogen fiwing and carbon fixing cells. Using GFP the team has showed that, at odds with several proposals, each cell possesses its own individual periplasm; however small molecule can be exchanged from one cytoplasm to its neighboring one.

Response to oxidative stress:

A Ser/Thr kinase, Pkn22, has been identified as being involved in the response to oxidative stress. The gene coding for this kinase is part of an operon which also encodes a putative peoxiredoxin and a putative cysteine desulfurase. These candidate genes have been characterized and shown to encode for a thioredoxin dependent peroxidase and cysteine desulfurase indeed involved in protection against oxidative stress.

During the evaluated term the team has published 28 articles in peer-reviewed international journals, out of which 19 are authored by team members as PI (1st or last author): 1 PNAS, 3 Mol Microbiol, 1 Appl. Environ Microbiol, 6 J Bact, 1 BBA-Bioenergetics, 1 Res Microbiol….The publication record of the team is excellent, especially when considering the fact that 3 full time researchers have ceased their activity druing the past term. The remaining

permanent members in the team has heavy teaching duties and one of them is remarkably involved in the Université de la Méditerranée (as Dean of the Faculty of Sciences).

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

The team leader is recognized at the international level as a leader in its field as witnessed by the invitation to several international congresses and its appointment as editor by several first rank journals in the microbiology field (J bact, Microbiology).

The team has strong and long lasting links with Shandong University in China. Due to this special relationship with China, the team has hosted several chinese PhD with one in a co-tutelle system.

The team has successfully apply for competitive funding: 1 ANR (PI), 1 ANR (partner), 1 Région PACA (PI).

- **Appreciation on the scientific strategy and the project**

The project is a continuation and an extension of the previous one and will include:

- site directed mutagenesis of the oxoglutarate receptor to obtain insensitive or hypersensitive mutants. Identification of the interacting partners,

- use of fluorescence probes to characterized the exchange of small molecules through the periplasmic space,

- transcriptomic analysis of the heterocyst development,

- characterization of the sulfiredoxin gene part of the Pkn22 operon, and elucidation of the function of the gene cluster,

- transcriptomic analysis of the response to ROS,

- cross talk between iron and nitrogen starvation.

- **Conclusion:**

  - Summary

The team, and more precisely its leader, is recognized at the international level as a very strong actor in the field. The scientific production is excellent, quantitatively and qualitatively. The main concern comes from the fact that since the retirement or departure of 3 CR during the last term, the team is now composed of 1 PR one honorary DR and 1 assistant professor. 1 Assistant professor and 1 IE are expected to be recruited in 2011. Despite the significant decrease of the task force, hardly compensated by the expected recruitment, the proposed project is in fact expanding to include transcriptomic approaches and crosstalk between iron and nitrogen starvation. Even though adding these axis is undoubtedly scientifically legetimate and should be encouraged and supported, the overall project may suffer from a lack of focus when considering the teaching duties of the team members.

  - Strengths and opportunities

The international recognition of the team and the wide range of approaches developped to tackle important biological issue is a strength. Despite the significant decrease of the task force, hardly compensated by the expected recruitments, the proposed project is in fact expanding to include transcriptomic approaches and crosstalk between iron and nitrogen starvation. Even though adding these axis is undoubtedly scientifically legitimate and should be encouraged and supported, the overall project may suffer from a lack of focus when considering the teaching duties of the team members.

  - Weaknesses and threats

The ratio between the size of the team of the wide scope of the project is weak.

Intitulé UR / équipe	C1	C2	C3	C4	Note globale
UPR9043 - LABORATOIRE DE CHIMIE BACTÉRIENNE	**A**	**A+**	**A+**	**A+**	**A+**
CYCLE PHAGIQUE ET MÉTABOLISME BACTÉRIEN [BARRAS-ANSALDI]	A	A	Non noté	A	A
ADAPTATION AU STRESS CHEZ LES ENTEROBACTÉRIES [BARRAS-BARRAS]	A+	A+	Non noté	A+	A+
ETUDE GÉNÉTIQUE DU MÉTABOLISME ÉNERGÉTIQUE D'ACIDITHIOBACILLUS FERROOXIDANS ET DE THIOMONAS SP [BARRAS-BONNEFOY]	A	A	Non noté	A	A
VIABILITÉ BACTÉRIENNE ET STRESS OXYDANT [BARRAS-DUKAN]	A+	B	Non noté	A	A
TRANSPORTEURS ABC CHEZ BACILLUS SUBTILIS: FONCTIONNEMENT ET RÉGULATION [BARRAS-FOGLINO]	B	B	Non noté	B	B
MÉTABOLISME ET DIFFÉRENCIATION CELLULAIRE CHEZ BACILLUS SUBTILIS [BARRAS-GALINIER]	B	A	Non noté	A	A
BIOGENÈSE DES MÉTALLOPROTÉINES ET RESPIRATION ANAÉROBIE CHEZ LES PROCARYOTES [BARRAS-MAGALON]	A+	A+	Non noté	A+	A+
BIOGENÈSE ET RÉGULATION DE SYSTÈMES RESPIRATOIRES ANAÉROBIES [BARRAS-MEJEAN]	A	A+	Non noté	A+	A+
BIOLOGIE CELLULAIRE DE LA MOTILITÉ BACTÉRIENNE [BARRAS-MIGNOT]	A+	A+	Non noté	A+	A+
ADAPTATION D'ESCHERICHIA COLI À LA PHASE STATIONNAIRE [BARRAS-MOREAU]	B	B	Non noté	B	B
GÉNOME, EVOLUTION ET BIOINFORMATIQUE [BARRAS-TALLA]	A+	A	Non noté	A	A
CELLULOSOMES ET DÉGRADATION DES POLYMÈRES VÉGÉTAUX [BARRAS-TARDIF]	A	A+	Non noté	A+	A+
ARCHITECTURE FONCTIONNELLE DES CELLULES BACTÉRIENNES [BARRAS-WU]	A+	A+	Non noté	A+	A+
DIFFÉRENCIATION CELLULAIRE MICROBIENNE ET SIGNALISATION [BARRAS-ZHANG]	A+	A+	Non noté	A+	A+

C1 Qualité scientifique et production
C2 Rayonnement et attractivité, intégration dans l'environnement
C3 Gouvernance et vie du laboratoire
C4 Stratégie et projet scientifique

Statistiques de notes globales par domaines scientifiques

(État au 06/05/2011)

Sciences du Vivant et Environnement

Note globale	SVE1_LS1_LS2	SVE1_LS3	SVE1_LS4	SVE1_LS5	SVE1_LS6	SVE1_LS7	SVE2 _LS3 *	SVE2_LS8 *	SVE2_LS9 *	Total
A+	7	3	1	4	7	6		2		30
A	27	1	13	20	21	26	2	12	23	145
B	6	1	6	2	8	23	3	3	6	58
C	1					4				5
Non noté	1									1
Total	**42**	**5**	**20**	**26**	**36**	**59**	**5**	**17**	**29**	**239**
A+	16,7%	60,0%	5,0%	15,4%	19,4%	10,2%		11,8%		12,6%
A	64,3%	20,0%	65,0%	76,9%	58,3%	44,1%	40,0%	70,6%	79,3%	60,7%
B	14,3%	20,0%	30,0%	7,7%	22,2%	39,0%	60,0%	17,6%	20,7%	24,3%
C	2,4%					6,8%				2,1%
Non noté	2,4%									0,4%
Total	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%

*** les résultats SVE2 ne sont pas définitifs au 06/05/2011.**

Intitulés des domaines scientifiques

Sciences du Vivant et Environnement

• SVE1 Biologie, santé
- **SVE1_LS1 Biologie moléculaire, Biologie structurale, Biochimie**
- **SVE1_LS2 Génétique, Génomique, Bioinformatique, Biologie des systèmes**
- **SVE1_LS3 Biologie cellulaire, Biologie du développement animal**
- **SVE1_LS4 Physiologie, Physiopathologie, Endocrinologie**
- **SVE1_LS5 Neurosciences**
- **SVE1_LS6 Immunologie, Infectiologie**
- **SVE1_LS7 Recherche clinique, Santé publique**

• SVE2 Ecologie, environnement
- **SVE2_LS8 Evolution, Ecologie, Biologie de l'environnement**
- **SVE2_LS9 Sciences et technologies du vivant, Biotechnologie**
- **SVE2_LS3 Biologie cellulaire, Biologie du développement végétal**