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

Department for the evaluation of research units

AERES report on unit:

Génomique Métabolique

Under the supervision of the following institutions and research bodies:

Centre National de la Recherche Scientifique - CNRS

Commissariat à l'énergie atomique et aux énergies alternatives

Université d'Évry-Val d'Essonne - UEVE

January 2014

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

Department for the evaluation of research units

On behalf of AERES, pursuant to the Decree of 3 november 2006[1]*,*

- Mr. Didier HOUSSIN, president
- Mr. Pierre GLAUDES, head of the evaluation of research units department

On behalf of the expert committee,

- Mr Bernard HENRISSAT, chair of the committee

[1] The AERES President "signs [...], the evaluation reports, [...] countersigned for each department by the director concerned" (Article 9, paragraph 3 of the Decree n ° 2006-1334 of 3 November 2006, as amended).

Evaluation report

Unit name:	Génomique métabolique
Unit acronym:	
Label requested:	UMR CNRS, CEA, UEVE
Present no.:	UMR 8030
Name of Director (2012-2013):	Mr Marcel SALANOUBAT
Name of Project Leader (2014-2018):	Mr Marcel SALANOUBAT

Expert committee members

Chair:	Mr Bernard HENRISSAT, University Aix-Marseille
Experts:	Mr Duccio CAVALIERI, University of Trente, Italy
	Mr Francis MARTIN, University of Nancy
	Mr Denis POMPON, University of Toulouse
	Mr Christoph STEINBECK, University of Cambridge, United Kingdom
	Mr Emmanuel TETAUD, University of Bordeaux
	Mr Nick TURNER, University of Manchester, United Kingdom

Scientific delegate representing the AERES:

Ms Sophie DE BENTZMANN

Representative(s) of the unit's supervising institutions and bodies:

Mr Gilles BLOCH, CEA

Mr Thierry GRANGE, CNRS

Mr Philippe HOUDY, Université d'Évry-Val d'Essonne

Mr Bernard PRUM (Representative of Doctoral School n° 423)

1 • Introduction

History and geographical location of the unit

The "Unité Génomique métabolique" laboratory is the research arm of the Genoscope, the French national sequencing facility established in Évry, France. This laboratory, which comprises approximately 75 persons (60 of which have a permanent position), specializes in the scientific exploitation of the wealth of sequence data produced by Genoscope. The unit is affiliated to three institutional bodies: CEA, CNRS and Université d'Évry-Val d'Essonne (UEVE), CEA being the main provider of recurrent funds and of permanent positions. The unit was created in 2000 and in 2008 Mr Jean WEISSENBACH (the founding director), was replaced by Mr Marcel SALANOUBAT but remained head of the Genoscope.

Management team

The director of the "Unité Génomique métabolique" is Mr Marcel SALANOUBAT, who has been the director of the unit for the last 5 years reviewed here and is proposed to continue for a second 5 year mandate. The director works with a formal Conseil de Laboratoire (composed of the leaders of each of the 7 teams that compose the unit of of representatives of the staff) and of more informal meetings with the heads of each laboratory who meet on a regular monthly basis.

AERES nomenclature

SVE1_LS1 Biologie moléculaire et structurale, biochimie

SVE2_LS8 Evolution, écologie, biologie des populations

SVE2_LS9 Biotechnologies, sciences environnementales, biologie synthétique, agronomie

SVE1_LS2 Génétique, génomique, bioinformatique

Unit workforce

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	5	5
N2: Permanent researchers from Institutions and similar positions	26	24
N3: Other permanent staff (without research duties)	29	27
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)		
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	6	6
N6: Other contractual staff (without research duties)	8	8
TOTAL N1 to N6	74	70

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	3	
Theses defended	9	
Postdoctoral students having spent at least 12 months in the unit*	6	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	9	14

2 • Assessment of the unit

The committee unanimously agreed that the submitted written document, organized by themes rather than by teams, made the evaluation more difficult, as several issues were not immediately clear such as the amount of work and funding in overlap with Genoscope, the exact contributions of each team, the overlap in the results of several teams and the overlap in their research projects. Because the oral presentations only partly clarified these aspects, the committee requested a document summarizing what were the exact major contributions of each team during the last 5 years and this useful document was handed to the committee on the second day after the discussion with the representatives of the governing bodies. The on-site visit has helped to clarify some of these points.

The committee was impressed by the support and interest of the University for this UMR, visible from the presence of no less than 4 persons including not only of the Vice-President for Research of UEVE, but also of the UEVE President in person. The committee also discussed with the representative of CEA (the main provider and driver of the UMR) and of CNRS. All institutions, regardless of their respective contributions appear to support fully the UMR. The CEA representative explained that translational research, IP protection and technology transfer are only a moderate priority for the CEA (in this UMR) and that CEA rather expects good science. This may explain the general lack of interest for these points in the UMR.

Conclusion

- **Strengths and opportunities**

Strengths : Overall the committee found that the competence and creativity of the scientists, engineers and technicians working in the unit translated into science, from very good to outstanding level, depending of the cases. The comfortable funding environment provided by CEA and the large number of permanent staff (mostly CEA, but also CNRS, UEVE and INSERM) clearly constitutes a major asset that can drive creativity and encourages risk taking. The position immediately downstream of Genoscope enables the direct translation of sequence data to functional discovery.

Opportunities : The Genoscope is still a major player in nucleic acids sequencing and this gives the unit a leader position in a number of projects such as the genomic and metagenomic investigations in the Tara project. The involvement and activity of researchers of the unit in national (France Génomique, Institut Français de Bioinformatique) and European (Elixir) networks on Bioinformatics are expected to provide novel opportunities. Finally potential synergies with ISSB are likely to derive from the proximity and complementarity of the two laboratories.

- **Weaknesses and threats**

Weaknesses : Possible weaknesses include unequal (and, for some, insufficient) international visibility of team leaders and team members and therefore of the unit as a whole. In line with this observation, the committee noted an unequal overall publication performance (whether considering the number or the impact). It was felt that several small groups lack critical mass and show leadership not as strong as large groups.

Threats : The golden age of sequencing is over, and hugely competitive sequencing facilities such as the BGI in China are now attracting massive amounts of research subjects. At a time when the country is trying to reduce public spendings, it is uncertain that the current funding levels will be maintained indefinitely. The internal organization of the unit appears moderately well adapted to funding restrictions/cuts and to competition with more aggressive laboratories.

- **Recommendations**

The committee believes that the unit should engage in a reflexion and internal review on how to organize itself better (i) to maintain the excellence of the well established groups and improve the international visibility of several of its members and leaders, (ii) to develop more contacts with the economic world in order to engage more into research subjects of significant economic value and of higher IP significance, and (iii) to identify and apply for alternative and competitive funding sources (H2020, ERC, industrial contracts, etc).

The three smaller laboratories LCAB, LCOB and LA would benefit from greater integration, particularly in terms of identifying strategic priorities and co-ordinating what are clearly overlapping interests and expertises. As an integrated entity, they should also develop a plan for raising their profile internationally, through publications, attendance at international conferences, organising meetings, exchange of students, participation in H2020 schemes. A combined grouping would also provide a stronger unit when approaching industry and trying to negotiate collaborations and funding from private sources.

Directors cannot do more than two consecutive mandates. In consequence a new director will have to be identified towards the end of the second mandate ofthe current director. Because of the constant changes in the technological landscape of genomics, it will also be a good opportunity to re-evaluate the organisation and articulation of the Genoscope and of the unit.

3 • Detailed assessments

Assessment of scientific quality and outputs

First of all the committee recognized that the evaluation addresses one of the laboratories of excellence in genomics and bioinformatics, well established not only in France but in Europe as a whole. The committee witnessed the remarkable competence and creativity of the unit staff. This is reflected by not only the funding of 25 ANR projects (LCAB, LGBM, LABIS, LABGeM, LMP), but also by the scientific production of the unit. With this said, exactly for this reason a structure like the one under examination is expected to perform better than an average laboratory.

The unit published approximately 230 publications during the 6 year review period (2008-2013), which corresponds to approximately 40 papers per year (1.3 paper per PI per year). This rather modest value masks disparities, with some teams more productive than others. In terms of impact, the situation is much better, pointing to one of the peculiarities of this unit, which seems to favor quality over productivity. Indeed during the reference period, the unit has produced a remarkable set of 9 papers in Nature and 2 in Science. In another estimate of the impact of the publications, the committee has found that the unit has produced an impressive 15 Nature 'equivalents' during the period examined (a Nature 'equivalent' is a paper that has received at least as many citations as the average Nature paper published the same year, regardless of the journal where the article was published). The distribution of these highly cited papers, however, is unequal with LABIS producing most of them, the others being assignable to LABGeM, LMP and LGBM.

In terms of external funding, the situation within the unit is unequal too, with impressive funding raised by LABIS, LMP and LABGeM, more moderate by LGBM, low levels of funding for LCAB, and none for LCOB and LA. Although it is not clear how much of the funds raised were assigned to Genoscope to perform the sequencing tasks, it is striking that the teams that rely heavily on experimental science raise less funds than those involved in Bioinformatics. This may constitute a weakness in the future when/if the level of funding of research was to decrease.

Assessment of the unit's academic reputation and appeal

The Genoscope umbrella and the outstanding productivity of the bioinformatics-centered laboratories have given the unit a reputation of excellence both nationally and internationally. Again, and this is a recurring theme in this report, the academic standing, reputation and appeal are unequally distributed within the unit.

Assessment of the unit's interaction with the social, economic and cultural environment

Given that the unit is involved in the sequencing of prokaryotes of biological interest for white biotechnology and of several agricultural crops, the number and intensity of the interactions with the industry is fairly low for all teams. The limited interactions with industry (and the associated limited number of patent applications, software deposition) appear to be a consequence of the lack of visibility of some teams and of the insufficient incentives to seek IP protection.

Assessment of the unit's organisation and life

The director of the "Unité Génomique métabolique" is Mr Marcel SALANOUBAT, who has been the director of the unit for the last 5 years reviewed here and is planning to continue for a second 5 year mandate. The visiting committee found that the personnel in the unit works in a peaceful and relaxed atmosphere and appears to fully support an organization where, thanks to ample funding, all consumable and equipment costs are paid for, regardless of whether there is external (national, European or industrial) funding or not for a particular research area. Another point of discussion was the 18 month limit to work contracts with CEA funds, which appeared to be the sole point of staff dissatisfaction that the committee found during the interviews. The committee was glad to hear from the CEA representative that the 18 month limit is to change soon to 36 months (for newly established contracts).

Discussions with the personnel revealed that the general organization is largely shared and agreed upon, whether by the permanent researchers or by PhD students and postdoctoral fellows, and that all personnel appears happy to work in the comfortable environment of the UMR.

Technicians, engineers and administrative staff were also generally very positive. Some wished to be better informed of the acceptance/publication status of publications, and to attend more seminars.

Assessment of the unit's involvement in training through research

As for the other evaluation criteria, the involvement in training through research was found to be of unequal intensity among the teams (from fair to excellent), and unlike some of the other parameters examined, this involvement does not correlate with team size. The committee is of the opinion that the number of PhD students and postdoctoral fellows could be increased, and the announced end of the 18-month rule for CEA work contracts should facilitate the hiring of new postdoctoral fellows.

Assessment of the five-year plan and strategy

The 5 year plan varies considerably across the contributing teams, e.g. in some cases it is essentially a continuation of ongoing work already underway whereas in other cases there is a greater degree of strategic planning involved. All teams should be strongly encouraged to develop a clear plan that addresses the comments made below in the individual laboratory assessments.

The plans for the next five years do not see major changes and can be essentially described as a logical continuation of what each group in the unit has already started. The committee acknowledges that the proposed areas of research are of high level with an appropriate level of risk-taking. The committee also recognizes that the 5 year plan develops an integrated research from genome (whether prokaryotic to eukaryotic) sequence to gene function and applications thereof. The ability to perform blue sky-research on basic science is one of the essential requirements to keep the current high publication and scientific impact of the unit as a whole. This ability is very much dependent on the continuation of a high financial support from the national public bodies. The competences of the lab members are particularly well adapted to the challenges, the only advice being to perhaps address the organizational aspects described below, in order to operate at the highest level.

During the last 5 years, the unit has enjoyed ample funding from its main provider (CEA) and from the dominating position of Genoscope as the sole sequencing center in France capable of embarking in large-scale projects. This unique financial situation has the advantage of providing a working environment particularly comfortable for the various teams of the unit. The unit is organized accordingly, with the sharing of resources (consumable and equipment) by all the teams. This organization, unusual these days, has a significant impact on how the teams and the unit operate. On the one hand, the comfortable financial situation of the laboratory allows the individual teams to embark on challenging subjects and therefore contributes to free creativity. On the other hand, the comfortable environment has some adverse effects such a transforming the unit into what could be described as a safe heaven, which isolates a bit the researchers from the drawbacks and advantages of the hugely competitive international research. Because the relative isolation from mainstream international research is becoming apparent for some of the teams despite undisputable competence and creativity, the committee recommends that the unit engages an assessment on how to organize itself to:

- Improve the international visibility of its members (there are obvious exceptions here such as the Genoscope director and the LABIS leader who are internationally acclaimed scientists);

- Develop contacts with the economic world in order to (i) engage into research subjects of significant economic value, (ii) secure more intellectual property and (iii) develop technology transfer;

- Identify alternative sources should ample funding and recruitment level decrease in the future, alas a possible scenario.

The committee also noted disparity in the size of the various teams composing the unit, with three fairly large groups (LGBM, LABGeM, LABIS), one middle size (LMP) and three small groups (LCAB, LCOB, LA). This disparity in size is accompanied by a disparity in output quantity and quality, largely due to the different nature of the activities (genome analysis & bioinformatics vs. wet lab approaches). Like the members of the unit did notice themselves, it is disappointing to note that experimental wet lab science is somehow less immediately rewarding than bioinformatics (analysis derived from inspecting the citations received by each paper published in the reference period). It may well be that this will come to an end since after the initial “boom” of genomics, large scale sequencing no longer requires an identified national sequencing center and is now widely available to any laboratory. The committee therefore fully shares the analysis made by the unit, namely that the next challenge in the disciplines of Biology, Chemical Biology and Synthetic Biology is to determine in an integrated manner the function of unknown genes and to exploit this knowledge to both fundamental and applied levels.

4 • Team-by-team analysis

Team 1: Laboratoire d'Analyse Bioinformatique en Génomique et métabolisme (LABGeM)

Name of team leader: Ms Claudine MÉDIGUE

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	6	6
N3: Other permanent staff (without research duties)	6	6
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	2
N6: Other contractual staff (without research duties)	5	5
TOTAL N1 to N6	19	19

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the unit	3	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	2

• Detailed assessments

Assessment of scientific quality and outputs

The LABGeM team has been successful in contributing to bacterial genome analysis and comparative genomics by developing computational tools that enable analysis of sequence data. This team has developed or participated in several projects in the unit among which the most visible were:

(i) the study of the metabolic diversity of *E. coli* strains which has been performed in the context of an ANR project (METACOLI). In this work they have built and analyzed the genome-scale metabolic networks of 29 commensal and pathogenic strains;

(ii) the discovery of new enzymatic activities in prokaryotes. Here LABGeM members have developed a new tool named CanOE, to analyze the conservation of genomic and metabolic context in order to predict candidate genes for orphan enzymatic reactions;

(iii) the study of the diversity of secondary metabolites in Cyanobacteria based on a large scale analysis of 126 cyanobacterial genomes and about 450 gene clusters;

(iv) the development of MicroScope bioinformatics platform including the simultaneous processing of several new microbial genomes, the modification of the web interface, the addition of several tools (RGP-Finder and Pathway curation) and the integration and analysis of RNA-seq data.

Over the review period, the team members have been very productive with participation to 96 high quality publications (among which PLoS Genet 2009, J Bacteriol 2011, BMC Genomics 2012, PLoS Comput Biol 2012, Microbiology 2013, PNAS 2013, Nat Genet 2013, NAR 2013, Nat Chem Biol 2014) including 16 articles with one LABGeM member at the first and/or last author position. In addition, many articles have been published in collaboration with other French or European groups.

Assessment of the unit's academic reputation and appeal

There is a real visibility of the team at the national level in the field of genomics/bioinformatics but the international visibility could be improved. During the review period, the team leader has been invited to give 2 invited talks in international research conferences and the group members gave 17 oral communications mainly in national conferences. This team has numerous national but fewer international collaborations. 12 research grants are listed as having been awarded during the review period but only one of these runs beyond 2014. The group managed to find European funding (PCRD microne) as well as national (8 ANR and 3 others) which also provides evidence that the works of this group are fundable in this area. This team also coordinated the National Bioinformatics Network (ReNaBi) from July 2008 to July 2012.

In summary, the LABGeM team is a well-recognized group in the French bioinformatics landscape, but does not achieve the international impact that its competence deserves. This is possibly due to frontal competition with large international organizations such as IMG/DOE, NCBI, EBI, etc., which aggressively develop tools for the annotation and bioinformatics analysis of genomes.

Assessment of the unit's interaction with the social, economic and cultural environment

The team leader participates in many scientific committees. The team has successfully obtained a service contract for more than 3 years and an R&D contract starting in 2014 with two important companies. The team also provides and develops MicroScope, an integrated Web platform for the annotation and the exploration of microbial genomes utilized by microbiologists.

Assessment of the unit's organization and life

The LABGeM team includes 5 researchers, 4 permanent engineers and technicians, 2 postdoctoral fellows and 1 PhD student. During the review period, the team recruited 2 researchers, 2 engineers, 3 post-doctoral fellows, 1 PhD student and 6 master students.

Assessment of the unit's involvement in training through research

The committee was unanimous to acknowledge the excellence of this team in terms of training through research. This is mostly the result of large training courses on the MicroScope platform (28 sessions organized in France and abroad for a duration of 4 days). In addition, 4 PhD theses were produced and defended over the review period.

Assessment of the five-year plan and strategy

The proposed project is largely based on the work of the previous years, and now LABGeM wants to develop new tools for the analysis of data through the MicroScope platform. Several aspects are considered, an analysis dedicated to metagenomic data, the discovery of new enzyme activities with the development of the CanOE tool, the modeling of metabolic networks and the optimization of the MicroScope platform with particularly the development of two new tools (PALOMA and TAMARA) to handle next generation sequencing data. These extensions are logical and the team has the competence to achieve solid results despite competition with aggressive platforms abroad.

Conclusion

- **Strengths and opportunities:**

The LABGeM team has a longstanding expertise and technical competence in his field. The team has a excellent scientific production reflecting an intense collaborative work, and a very good publication record both in terms of quality and quantity. The group leader is very well integrated at the national level, and has numerous collaboration with other groups in the unit.This is probably one of the best research group in genomics/bioinformatics in France.

- **Weaknesses and threats:**

There are no major weaknesses identified with the exception of the international dimension which could be improved. In addition, only one person in the team is habilitated to mentor PhD strudents (HDR) which is relatively low for the size of the team and the number of researchers.

- **Recommendations:**

The committee recommends to improve the international visibility of the group by increasing the number of oral presentations in international meetings and by the recruitment of foreign postdoctoral fellows. It might be interesting to benchmark the MicroScope platform against other services abroad and identify its strongest features to communicate in a more aggressive manner and contribute efficiently to the larger European infrastructure on microbial genomics resources. The committee encourages the group to continue its efforts.

Team 2: Laboratoire d'Analyse Bioinformatique des Séquences (LABIS)

Name of team leader: Mr Patrick WINCKER

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	8	7
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)	1	1
TOTAL N1 to N6	12	11

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		
Theses defended		
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	3	2

• Detailed assessments

Assessment of scientific quality and outputs

A large part of the work of the team has focused on the genome evolution in crop plants, such as cacao, banana, coffea and rapeseed. This work has had considerable impact on the scientific community. This work has led to the production of exciting findings on the polyploidisation in Angiosperms. The team has also highlighted novel mechanisms driving the evolution of genomes in asexual animals (*Adineta vaga*). The team has also been involved in several projects of comparative genomics in plant-interacting fungi and algae, although these studies were carried out in large consortia where the team was not leader, but provided their unique expertise in genome sequencing and analysis. Finally, the team is a driver in the mega-project TARA Ocean aiming to survey the (meta) genomic variability in marine ecosystems. This cutting-edge science provides new insights on the genomic diversity of marine eukaryotes. In total the team members have published 66 indexed articles of which most are signed by team members as first or last authors. These articles are complemented by non-indexed publications, book chapters and articles in conference proceedings.

The quality of the journals in which the work of this team publishes its own work is generally excellent, with a number of outstanding contributions articles in Science, Nature Biotechnology, Nature Genetics, Genome Biology, Genome Research, PloS Genetics and PNAS. In terms of true citation impact, the team has published 10 of the 15 Nature 'equivalents' produced in the UMR. Despite this clear leadership, the LABIS team is only weakly engaged in translational research.

Assessment of the unit's academic reputation and appeal

LABIS contributes strongly to the large number of high visibility publications of the unit and therefore contributes to a large portion of its international visibility and, by extension, of Genoscope. The LABIS Team is also extremely active in multiple international collaborations. The LABIS team is undoubtedly a world leader in eukaryotic genomics. They have provided a tremendous resource to the various communities working on higher plants, algae and fungi. The team has benefitted from multiple international research contracts and has participated as a partner in several European projects, as well as acting as either coordinator or partner in several international contracts. At the national level, the Team has coordinated or was involved in 9 ANR grants during the review period.

The research of the group into the eukaryotic genomics has led to 38 invited talks (mainly international), underlining the broad interest that this work has attracted. In addition, members of the group have been solicited to participate in national and international level evaluation committees.

Team members have been implicated in outreach at the more local level, for example a researcher has spoken about genomics at Universciences. They participated to an excellent documentary on the TARA expedition broadcasted on the ARTE TV channel.

Assessment of the unit's organization and life

The LABIS team counts 8 permanent researchers (6 from CEA and 2 from INSERM), one engineer and one technician. The number of non-permanent staff is limited to one postdoctoral researcher and one engineer.

Assessment of the unit's involvement in training through research

Team members have organized and participated in several valuable training genomic workshops and practical courses for researchers, graduate students and teaching staff at the Genoscope and partner institutions. However, during the evaluation period, the LABIS team has supervised a very limited number of post-doctoral fellows (only two) and no PhD. The expertise of the team in sequencing technologies and genome analysis is unique and the committee is convinced that dozens of highly motivated students would be willing to work in this team. In the future, the LABIS team should be encouraged to host students and young scientists from the TARA consortium.

Assessment of the five-year plan and strategy

The group will not undergo major changes for the next evaluation period, and research projects are mainly continuations of ongoing large-scale projects, such as TARA Oceans program, for which funding appears to be largely in place. The LABIS team underlines their evolution towards the analysis of marine biodiversity using NGS based metagenomic approaches set during the previous evaluation period, and proposes to continue in this vein. They will also investigate the structure and evolution of the genome from marine eukaryotes, such as protists.

The project aiming to develop *in silico* approaches to characterize orphan genes in marine eukaryotes is very challenging, and would provide a major breakthrough if successful.

Although scientifically well justified, and feasible given the considerable expertise of the team, there is a lack of emphasis in the potential applications of the outcome of the research of this group (e.g., could the metagenomic analyses produce biomarkers to assess marine ecosystems ?).

Similarly, very little information was provided regarding the social or economic impact of the research on crop plants. Given that the work of the team has considerable potential in terms of the identification of potentially valuable targets/markers for genetic improvement in several crops important to developing countries, this is an area which could be strengthened.

Conclusion

During the evaluation period, the LABIS group has demonstrated an impressive leadership in eukaryotic genomics and is clearly one of the most visible worldwide.

- **Strengths and opportunities:**

The LABIS team is a leader in sequencing technologies, genome analysis, comparative genomics and eukaryotic genome evolution. This translates into an impressive array of top-level publications. The involvement of the LABIS team in the TARA Oceans program provides the laboratory with unique discovery opportunities on the evolution and function of marine eukaryotes.

- **Weaknesses and threats:**

The absence of PhD students, the limited number of postdoctoral scientists and lack of translational research can be perceived as a possible weakness. Sequencing technologies can be considerably cheaper in other sequencing centers; the LABIS team thus appears somewhat dependent on national funds.

- **Recommendations:**

In a near future, the project dealing with *in silico* characterization of orphan genes in marine eukaryotes should perhaps be connected to 'wet bench' characterization of the unknown proteins through functional analysis. This would have the further advantage to strengthen the interactions of LABIS with the other teams of the unit.

It is unclear if only bioinformatics and sequencing without proper phenotypic and model testing will allow such a successful laboratory to keep the pace with the fast advance of genomics. The committee is of the opinion that there is a strong need of strategic thinking ahead to evaluate the next big challenges and the research niches where the efforts should be focused. Also the scientific vision has to be accompanied by an evaluation on how the center can keep the pace with the rapid technological developments. LABIS would benefit enormously of the combination of high throughput and long reads, as well as from high throughput phenotyping, so it would be nice to see in which technologies and approaches LABIS wants to invest and where strategically LABIS wants to put himself in Europe and in the world. Clearly this strategic evaluation goes beyond LABIS itself and includes Genoscope.

The team leader could successfully apply for an ERC Advanced Grant.

Team 3 : Laboratoire de chimie organique et biocatalyse (LCOB)

Name of team leader: Ms Anne ZAPARUCHA

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	3	3

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The laboratory for organic chemistry and biocatalysis (LCOB) interested in understanding biocatalysis working with enzymes discovered in the unit in collaboration with LABGeM, LCAB and LGBM. The team both aims at using enzymes for improving organic synthesis as well as at utilizing organic synthesis to understand enzyme function. They also interact with LA with a view to improving biocatalysts via protein engineering/directed evolution approaches.

The team pursues laudable and interesting projects to understand a number of enzymatic model systems (nitrilases, racemases, and alpha-KAOs). The projects are ambitious, well-conceived and conducted. The future plan is largely to continue the existing projects. Of particular interest are the projects concerning dioxygenases and amine dehydrogenases, both of which address contemporary challenges and if successful will result in high impact publications which will raise the profile of the group internationally.

The team was established in 2008 but for the first year the team leader was the only team member. Only in 2009, first additional team members were hired. The late assembly of a critical mass in the group (and this critical mass is still not achieved) also partly explains the low publication output of the team. In the 6 years under review, the team published only 6 papers with only two of them as first or last author. The journals are in the medium (Tetrahedron Letters IF 2012: 2.376, Journal of Natural Products IF 2012: 3.285, Journal of Bacteriology IF 2012: 3.177) to High (Organic Letters IF 2012: 6.142, PLOS One) impact factor range. Clearly, the Nature Chemical Biology (IF 2012: 12.948) paper is the highlight of the short publication list. Only one of the papers was co-authored by one the PhD students and as far as the committee could see, none of the other interns (masters and engineering students) work resulted in a publication.

The work the LCOB group performs in collaboration with other groups in the unit is very good and essential. Some aspects of the work of this group are more service like in nature and in that respect the laboratory acts as a valuable support group. This is not a problem in itself but must be considered when evaluating the work in a scientific review.

Assessment of the unit's academic reputation and appeal

It is unclear from the documentation if the unit and its group leader has any wider scientific visibility. Certainly, the output of the group alone is not sufficient to build a wider academic visibility. The organization of the 24ème colloque du Club Bioconversion en Synthèse Organique, CBSO, is noted as a highlight of LCOB in the five year period evaluated. The panel noted that, while the number of people attending was high, the title implies a purely French exercise which again is not suited to build an international recognition and appeal. From the interview during the evaluation, the panel got the impression that there is very little spirit for expansion and outreach and to build a scientific reputation for the group leader.

Assessment of the unit's interaction with the social, economic and cultural environment

The group has filed a patent application on the hydroxylation of amino acids with an amine-containing side chain by novel dioxygenases and the utilization of the products as chiral blocks for organic synthesis.

During the last five years, the interactions of the group with the social and cultural environment were essentially limited to local (Évry, Saclay, Paris) events, with the exception of an oral communication in the Biotrans meeting in Manchester, UK.

Assessment of the unit's organization and life

Since 2010, the team consisted of the team member, a scientist and a technician and hosted 2 PhD students, and 6 master and engineering students. The team seems to be well embedded in the institution which is demonstrated by the number of in-house collaborations, which seems high given the low number of group members.

Assessment of the unit's involvement in training through research

Two PhD and 6 master students supervised is a very good performance for a recently established team of the size of LCOB.

Assessment of the five-year plan and strategy

The 5-year plan addresses contemporary themes in biocatalysis, especially the development of new biocatalyst reaction platforms (e.g. C-H activation, region- and stereospecific hydroxylation, etc.). These themes are of significant interest for the industry. This is a laudable aim and if successful will result in high impact publications. However, the group also needs to consider expansion of its work, integration with LCAB and LA, and also greater engagement of industry. In particular, the involvement in international research consortia as well as bi- and tri-lateral international collaborations is recommended to build a wider recognition for the group.

Conclusion

The LCOB group is a recently established team led by a professor at UEVE. The group works on themes of interest in the field of Biocatalysis, and these themes and approaches are nicely complementary to what developed in other groups of the unit, particularly LCAB and LA. The overall production of LCOB, however, could be higher in volume.

- **Strengths and opportunities:**

The group shows a very good ability to identify interesting research subjects in the field of biocatalysis and it is clear that the group has the expertise and know-how to achieve significant results in themes of significant interest for the industry. More international visibility could be built through collaborative research projects with partners outside of France.

- **Weaknesses and threats:**

This relatively small group is under resourced and lacks higher level integration with the two complementary teams LCAB and LA. The group leader needs to engage more with the international research community.

- **Recommendations:**

This small team should attempt to work towards a higher internal integration. Independently of this, the group members should raise their international visibility through the more systematic publication of the work performed by students and through attendance at major meetings. Participation in international research consortia is highly recommended. The interactions with industry have room for improvement and development. Overall the group could be more aggressive when presenting its results, whether in terms of publications, attendance to meetings or when evaluating intellectual property.

Team 4: Laboratoire de Génomique et Biochimie du Métabolisme (LGBM)

Name of team leader: Mr Marcel SALANOUBAT

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	3	3
N2: Permanent EPST or EPIC researchers and similar positions	7	6
N3: Other permanent staff (without research duties)	4	6
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	2
N6: Other contractual staff (without research duties)	2	2
TOTAL N1 to N6	18	19

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	4

• Detailed assessments

Assessment of scientific quality and outputs

The team works on 4 complementary axes: metabolomics, molecular biology/biochemistry, biomass degradation and metagenomics/ enzyme discovery. The two major aims of the team are to improve knowledge of metabolic function in prokaryotes through gene and metabolic centric approaches and to improve functional annotation in public database by providing experimental evidence on function. These questions are addresses through a large number (16) of ongoing projects, most of them through internal collaborations within the unit.

Research studies of the team thus tightly match the global approaches of the unit and relative contributions to publications of the different partners are sometimes difficult to decipher. The originality of the LGBM team is to be more specifically involved in the biochemical screening and characterization of genes with poorly defined or unknown functions in relation to their roles in metabolic pathways. One focus lies in the identification of missing steps in metabolic pathways leading to the discovery of new functions.

This was particularly the case for the identification using metagenomic data mining of a gene involved in an alternative pathway of lysine fermentation (LGBM/LCOB). Similarly, the function and the mechanism of 3-keto 5-amino hexanoate cleaving enzyme was investigated and the 3D-structure determined through external collaboration. Other works addressed the identification of convergent evolution between non-homologous enzyme families in the methionine biosynthesis pathways and the correction of miss-annotations. Complementary to expression approaches, generation of collection of single-gene mutants was developed on the soil bacterium and applied for to investigate uric acid degradation in bacteria. New genes for a hidden catabolic pathway (trigonelline degradation) were identified. Metabolomic analysis involving LC-MS approaches were also used to investigate quinate metabolism. A second group of projects, which targeted the exploitation of life chemical diversity, led to the discovery of several new catalysts including aldolases using hydroxypyruvate. Targets of potential industrial interest: nitrilase and alpha-ketoglutarate dependent dioxygenases and Baeyer–Villiger monooxygenases were particularly investigated. Another project addressed clean-up of polyaromatic hydrocarbon involving two gene clusters of deltaproteobacteria. LGBM was also involved in orthogonal biology approaches like the substitution of thymine by isomorph 5-chlorouoracil in *E. coli* or in alternate approaches for carbon dioxide fixation in the same organism by developing an artificial capture cycle not involving the classical Rubisco system.

Globally the scientific production of the team is sound and the publications (26 papers over the period) appear frequently in high (JMB, JBC, PlosOne, etc) or sometime exceptional (Nature, Nature Chem. Biol.) journal ranks. However, it is noticeable that the best publications are frequently highly collaborative and, with few exceptions, signed at intermediate authorship positions. This indicates that the team is well integrated and plays an important role into ongoing unit researches but does not necessarily have a leadership position.

Assessment of the unit's academic reputation and appeal

Contrasting with the high rank of publication journals, the number of oral communications as invited speakers is fairly limited. Of the 8 listed, only 2 were in international meetings (3 additional including 1 international from a member are listed in the LCAB part) supporting the idea that the visibility of team members does not completely correlate with their publication output. Concerning expertise and participations to scientific committees, there is some participation to administrative tasks of UEVE/UFR SFA and a limited number of punctual expertise actions for French structures. There is no significant participation to ANR or evaluation European panels.

Collaborations outside the unit are mostly with French partners. Besides recurrent CEA funding, four external research contracts were obtained from ANR, EU, CEA (GENOZYME, Magic-Pah, Rbuce-up and Metatarget). Globally visibility of the team is mainly national contrasting with publications of high international quality. Members are already collaborating in association with LCAB with a German academic group (University of Frankfurt) and directly into two others academic collaborations (Russia, United Kingdom). Visibility of the team would benefit from more collaborations with European groups of high international visibility.

Assessment of the unit's interaction with the social, economic and cultural environment

There is no report or project of patent applications or licenses. This contrasts with what would be expected from a research group strongly oriented toward the discovery of new activities and missing steps in metabolic pathways of interest for industry. Similarly, the team does not seem to be involved as major contributor into any industrial contract. Considering the high potential and quality of the research performed, the interactions with socio-economic environment could be significantly improved.

Assessment of the unit's organization and life

The team is fairly large, with 16 permanent members mostly from CEA, 2 contractual researchers and 2 PhD students. Others major contributors to human resources are CNRS (1 DR2) and University of Évry (3 junior professors (MCU) and a contractual researcher). The number of permanent staff remained fairly stable over the reference period and no major change is expected in the short term.

Assessment of the unit's involvement in training through research

The team exhibits a fairly limited activity in education by research as judged by the number of PhD theses and post-doctoral stays: a single thesis has been defended during the reviewed period and a second defense is expected for the fall 2014. A new student has been recruited in 2014. At the post-doc level, a single 2 year stay has been reported. The training through research activity is more pronounced at the master level with 7 students (6 months stay) over the reference period. Several short terms stay of students at different pre-master levels are also reported. Globally, the activity of education by research could be better considering the team size. There is no report of pedagogic work involving team members, and no evidence of dissemination action for scientific knowledge, a situation contrasting with several other teams of the unit that perform better on this criterion. Team members are not involved in training network but two of its members were punctually involved in seminars of doctoral schools or organization of visits. One team member has supervised the Évry-Genopole participation of students to the iGem competition.

Assessment of the five-year plan and strategy

The organization of research project fully parallels the report section and appears mostly a direct continuation of ongoing projects. Among inflections are: (i) the development of research related to plant biomass fermentation to ethanol and hydrogen; (ii) the discovery of novel activities through new strategies that could benefit from the interaction with the ISSB unit in Évry, thus combining predictive bioinformatics with experimental validations; (ii) the cascade combination of different types of original reactions both for chiral resolution and building block constructions. Among the perspectives is the development together with the LA team of engineered organisms able to capture carbon dioxide. This last theme is clearly among the priorities of CEA around renewable energies and carbon cycle. However, a clearly established strategy was difficult to delineate in the written document and was not fully clarified by the visit. This leaves open the question of the general organization (assignment of manpower to research subjects and level of priority of this particular project) within the unit. The question would not be so critical for pure academic research, but an integrated and realistic strategy coupled to well defined resources are necessary to compete at the international level with top level research teams and major companies.

Concerning more specifically the work program of LGBM team, the current profusion of approaches, even if individually of interest, potentially leads to dispersion with dilution of resources on many targets. Particularly it can be questioned whether research fields must be focused around specific (currently a multitude) basic questions or, in contrast, try to address specific needs in terms of economic competitiveness, renewable resources, green chemistry or else. The environment of Genoscope and ISSB is very rich but poorly valorized in terms of economic impact. Particularly the synthetic biology approaches that appear within the work program could be developed in tighter partnership with iSSB but not only. Some research fields like the valorization of natural resources for the production of chemicals, biofuels or hydrogen and carbon dioxide recycling are already intensively studied in other French (including INRA, CNRS, IFPEN) and European centers. It is surprising that the project does not include any strategic consideration about competitive ongoing researches and the way to define complementary and collaborative strategies taking advantage of the unit capability and environment.

Conclusion

The team is managing a large number of complementary and collaborative approaches, fully-embedded into the unit research themes. However, its visibility and attractivity can be improved.

- **Strengths and opportunities:**

The strength of the team clearly stems from its multidisciplinarity and its experience in the expression and the biochemical characterization of genes of unknown functions involving complementary approaches. Another strength resides in the fact that the activities of the team are fully embedded in the unit's strategy and most of projects are highly collaborative. The publication level is excellent at the level of the journal rank. Opportunities are to better exploit the complementarities of approaches and known-how with ISSB and to build national and European partnerships around synthetic biology.

- **Weaknesses and threats:**

The interaction with economic partners is very limited, which is particularly surprising if one considers the large potential of the research subjects. This is a potential weakness and could constitute a threat if public resources decrease and become limiting.

From the academic side, while publications are generally performed in first rank journals, the international visibility of the team remains limited. This could result from the fact that team research is mainly collaborative within the unit making difficult for external people to evaluate the real contribution of team members.

The thematic dispersion of the team is clearly a threat precluding to reach critical mass on a specific question. This is particularly a preoccupation if the team wishes to enter application-oriented researches into very competitive fields.

Research program is clearly constructed when continuation of current work is concerned but strongly lack vision of the national and international contexts for the new objectives.

- **Recommendations:**

The team is managing a very large number of projects being at a key position in the unit for bridging genomic and functional approaches. This large number of projects makes it difficult to reach critical mass when competitive projects are concerned. The research program appears to lack rupture strategies and would benefit from a re-evaluation that would take into account international competition, the rapidly evolving state of the art in the biotechnology field and the focus on a more limited number of internationally competitive research questions. Other recommendations could include (i) opening more to the socio-economic environment with a suitable balance between basic and application oriented tasks; (ii) the involvement in national and international collaborations with high visibility groups, searching for complementarity and exploiting local environment above the limits of the unit and of Genoscope; (iii) a strong effort to continue attracting and incorporating young talents from abroad and to reinforce formation by the research.

Team 5 : Laboratoire de Métagénomique des Procaryotes (LMP)

Name of team leader: Mr Denis LE PASLIER

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	3	3
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	7	7

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs

First of all the committee agreed that the evaluation addresses one of the laboratories of excellence in microbial genomics and physiology, in one of the best genomics and post genomics centers in Europe. This is clear from the number and the level of the scientific production. With this said, exactly for this reason a structure like the one under examination requires to set the bar quite high with respect to an average group. The focus on metagenomic approaches to phenotypic microbial diversity is one of the strengths of the team. The contribution of the group is different in the different projects, therefore it was necessary to perform a precise assessment of projects and of the performance of the team in these projects to identify which projects are clearly under this group's leadership and which are collaborative efforts where the group gave a significant contribution but is not the main driver.

The Cloaca Maxima project is clearly the hall of fame of the team and is a nice example of integration of genomics physiology and bioinformatics. The metagenomic approach undertaken is limited by the techniques used so far. Despite the use of sophisticated bioinformatics tools calling unknown genes and assembling unknown genomes is still a very difficult task. In the committee's opinion, the project would benefit enormously from using novel sequencing methods enabling long reads and the sequencing of functional genes (RNA-Seq).

The Nitrogen cycle project, which is related to bacteria that play a key role in the nitrogen cycle, highlights the excellent microbiological skills of the group. Complete genome sequences were obtained from enrichment cultures, as a result from collaborative projects between LMP and groups in Wien or Nijmegen. This led to success and three very high impact publications in the field (PNAS, 2010; ISME J, 2012; Nature, 2010), the third of which is the most influential. The excellence in the results is clearly a product of the team capacity to interact successfully with well-established groups in the field.

The Arsenic contaminated sediments (LMP/LABGeM/in collaboration with group in Strasbourg) project is a very solid metagenomic analysis applied to the reconstruction of the genome of five previously unknown uncultivated bacteria. An excellent molecular microbiology work that shows the strength of the group in integrating metaproteomic data with biochemical functions, the work is very well described in a ISME J paper where the LMP team leader is last author, showing the strength of this team. Again the vision of what's next and why this is important for the development of the center would help understanding how the group plans to harvest the fruits of these excellent publications.

The Human gut microbiome (LMP in collaboration with INRA in the frame of EU-FP7) reported in (Nature, 2010, Nature, 2011) research is the only one supported by an international EU grant, MetaHit (Grant N° HEALTH-F4-2007-201052). The role of the LMP was mostly in the generation of fosmid libraries (used for functional analysis) and in coordinating part of the metagenomics (Sanger, 454 Titanium reads). The remaining sequencing was largely carried out in China by the BGI. The project funded by is one of the most successful EU projects carried out so far, limited possibly by the lack of development of an European equivalent of BGI and by the development of bioinformatics tools, two aspects in which in Genoscope should possibly regain leadership.

The main contribution of the unit to the Soil metagenome (LMP/collaboration with École Centrale de Lyon) project (ISME J, 2012) was to optimize the metagenomic approach by construction of fosmid libraries and development of microcosms with stress conditions methods, to enrich these samples in scarcely represented species. Again this is a project that underlines the excellent molecular microbiology skills of the team and the ability to contribute importantly to the success of team research efforts.

Assessment of the unit's academic reputation and appeal

The team is well established and well recognized overall, the scientific originality of the work and the level of institutional funding enables them to pursue frontiers research in fields where competition is not the main driver. The Médaille d'Or du CNRS attributed to one PI of the team (the director of Genoscope), the highest scientific recognition in France, crowns their reputation. The laboratory is internationally recognized as one of the most productive and innovative, mainly thanks to the number of international presentations related to the immense visibility of the director of Genoscope. Yet the appeal and ability to attract foreign researchers, postdoctoral fellows and PhD students to work in the team and in the unit could be improved given the high level of the science produced. There are 4 major European collaborations (Njimegen, Hamburg, Vienna and the Russian academy of science), and there is a major EU consortium where the LMP has taken a major role, MetaHIT.

Assessment of the unit's interaction with the social, economic and cultural environment

The LMP team is extremely well integrated within the national scientific community, with excellent interactions with the scientific and cultural environment. The Cloaca Maxima and the Chlorodecone projects have important potential impact on the society and have relevant environmental and health related applications. Yet the economic exploitation of the results could be improved by an intellectual property (IP) protection strategy and a technology transfer plan that are currently absent.

Assessment of the unit's organization and life

The organization chart shows that the LMP team is exclusively made of permanent staff, namely 3 researchers (one from CNRS, two from CEA), one university faculty, one engineer and two technicians. One of the two CEA researchers is the director of Genoscope.

Assessment of the unit's involvement in training through research

Two PhD students obtained their PhD during the 5 years period. Thus, PhD and postdoctoral training does not appear to be a clear priority for the team. A greater effort in internationalization of the research would indeed help in increasing the attractiveness of the LMP team and, for when the director of Genoscope retires, in maintaining its international visibility. Involvement in Marie Curie ITN actions may help to get funding and attract PhD students.

Assessment of the five-year plan and strategy

The five years plan shows that the LMP team will follow up on the latest scientific discoveries in metagenomics and subsequent applications to enzyme/pathway discoveries in microbial communities. More specifically, the team shows a plan for improving metagenomic approaches with the development of a hybrid binning/assembly based method for reconstructing genomes from metagenomic datasets. This method, which could be of general usefulness, will be applied to data from the MetaHIT initiative and to metagenomics data derived from microbial communities able to breakdown polyaromatic hydrocarbons (PAH) in soil, groundwater and marine sediments. On the experimental exploitation side, the group will continue the Chlordecone project (where the functional tests should be strengthened) and develop new tests for the discovery and characterization of critical enzymes for PAH degradation.

Conclusion

- **Strengths and opportunities:**

Overall the group is extremely successful and well integrated in the unit. This team performs mainly academic research, its focus is very well defined since it limits the activity to hard core microbiology and metagenomic approaches to prokaryotes. The ability to take on difficult and risky projects is indeed a strength of this team and will provide novel opportunities. The number of projects where the team is involved is sustainable given the resources available.

- **Weaknesses and threats:**

The LMP group's focus on molecular microbiology-microbial physiology-metagenomics can be seen as a strength from a scientific point of view, but also as a potential weakness. The group leader is very well established and successful in his field, but a potential shortcoming of the group is a lack of leadership in broader projects where it is involved. This is reflected by the fact that, despite the excellent overall publication record, the group leader has only two last author papers in the period analyzed (and not in the most influential papers, he participated to). There is no translational plan and activity, nor has the group generated patents or protected IP. Yet the group makes relevant research with industrial potential. The group could have a greater impact on the development of the socio-economic landscape in the region.

There could be a decrease in international visibility of the group when the director of Genoscope retires.

- **Recommendations:**

It is extremely difficult to give recommendations to a group like LMP. From a scientific point of view, the group could perhaps use more systems-level modeling approaches, integrating better metagenomics data with functional information. The somehow conservative approach dealing with solid hard-core microbiology paralleled by biochemistry is an asset and the group is indeed extremely helpful to the success of the institution as a whole. Despite this, a deeper insight in the data generated using the most recent bioinformatics tools could lead to the construction of models of how the organism functions and increase the impact of the authors' original work. Such an approach would also help the training of the PhD students in developing interdisciplinary skills. The committee also recommends an effort in improving the interaction with international research in the field of environmental metagenomics through international training programs and participation to grant applications in the H2020 and ERC framework. Though it is quite clear what's next in the future of this team, a more detailed description of the vision for the future development of the group would have helped the assessment and the evaluation of future directions for this team, and might help economic exploitation of the results. The group could invest more in dissemination of the results, training and outreach.

Team 6 : Laboratoire des Applications (LA)

Name of team leader: Ms Madeleine BOUZON-BLOCH

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	3
N3: Other permanent staff (without research duties)	4	4
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	6	7

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		
Theses defended		
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions		1

• Detailed assessments

Assessment of scientific quality and outputs

The team targets development of applications through synthetic biology approaches and is specifically involved into the set-up and servicing of coupled fluidic systems adapted to continuous culture of microorganisms for long period under controlled constraints. This part constitutes a platform activity involved in different projects of the unit.

The scientific output over the reference period consists into a limited number (5) of co-authored papers. Four of them being published into journals of medium impact factors (2.4-5) but one in the top ranked journal Angewandte Chemie. However, all papers were always signed at intermediate positions, not indicative of a leading contribution. The audition evidenced that the team is indeed involved in several common projects of the unit, playing an important role in developing and managing a platform dedicated to directed evolution of whole microorganisms. Collaborative works with other unit members mainly consisted to engineer and to evolve bacteria for the use of 5-chlorouracil instead of thymidine (LABGeM/LGBM collaboration) and to implement and characterize a non-canonical cycle for carbon dioxide fixation in *E. coli* by associating rational engineering and directed evolution *in vivo* (collaboration with LGM).

Based on oral presentation, the LA team is expected to play in the future a leading role in developing applicative fields of the unit. However, current publications, reports or presentations do not give yet an objective demonstration of the capacity of this small team to play the expected role. Particularly, the real scientific contribution of the LA team in these collaborative projects is difficult to define. On the technological side, an operational device for microorganism evolution under constraints was constructed using classical coupled fermenter technologies. However, the team does not seem to interact with external partners developing similar or alternate technologies including highly promising approaches based on micro- or milli-fluidic systems. Thus, while constructed devices fulfill a technological need of the unit, their developments cannot be considered as really innovative.

Assessment of the unit's academic reputation and appeal

Surprisingly enough for a team expected to be dedicated to applications, neither the written report nor the oral presentation gave indications of specific actions directed toward the socio-economic environment. There is no reported action on the dissemination of scientific knowledge or of participation of team members to scientific or evaluation committees, nor organization of scientific event or participation to an editorial board. A single oral presentation in a local (Évry) French meeting is reported. The team was not directly involved as initiator or major contributor into any external academic or industry related contract and external collaborations are not described.

The team has not obtained EU or ANR funding during the period. The lack of PhD students leads to questions regarding attractiveness of this group. No talks at conferences at national or international level were reported.

Globally, it appears that the national and international visibility of the team is extremely limited outside of its very local environment. Even considering its technical and likely significant role for the unit, the absence of collaborations with other external groups developing macroscopic or (micro)fluidic continuous culture devices is unfortunate and raises the question of the national and international competitiveness of the tools developed.

Assessment of the unit's interaction with the social, economic and cultural environment

Very little engagement « grand public », except a contribution that appears in the newspaper “Libération”. There is no output as patent application or identified valorization action in the report.

Assessment of the unit's organization and life

The team counts 6 members (2 researchers, 4 technicians or engineers).

Assessment of the unit's involvement in training through research

This point appears weak. The LA team reports only a time-limited co-direction (7 months) of a single PhD student over the reference period. No PhD defense is reported. Whilst here is no report of post-doctoral training, supervision of two engineers for 4 and 6 months respectively is mentioned. No other action relative to training through research is reported.

Assessment of the five-year plan and strategy

The project is centered on the continuation of works targeting selection and molecular characterization of 5-cholorouracil dependent strains and on further development of alternate carbon dioxide fixing pathways in bacteria. Perspectives of the work on 5-chlorouracil tolerant bacteria initiated by a former team member are uncertain and current LA team members are not co-authors of a recent high rank publication in the field involving the neighboring ISSB laboratory. Metabolic engineering to set-up alternate carbon dioxide capture pathways in bacteria is, in contrast, a promising, but very competitive field at the international level. The project seems to be rather more a collective approach of the unit than a project driven by LA.

A role of the team in participating in the development of genetic screens and tools for the design of new catalysts by *in vivo* directed evolution and the selection of alpha-ketoglutarate dependent dioxygenases is also suggested in the written documents. However, it remains unclear whether the team could in the future really reach a leader role in the development of such projects or would mainly continue to act through internal collaborations by managing specifically the *in vivo* evolution parts of these collaborative projects.

Conclusion

The team played a well-integrated and useful technological role in the unit, although without playing a clear driver role and establishing a visibility. Its role in the development of applications is expected to be strongly reinforced according to the unit work program.

- **Strengths and opportunities:**

The team certainly plays a technical and expertise role in contributing to common projects of the unit. Based on the unit project, the team would be expected to take in the future a leading role to bring knowledge to applications. However, its capability to successfully drive original synthetic biology projects remains to be demonstrated and might be not so realistic considering its small size. Opportunity would be clearly to elaborate a structure of more critical size taking advantage of the technical complementarity of LA, LCOB and LCOB members. In addition, it appears critical that technological requirements of the unit projects could be fulfilled not only by internal platforms but also optimally exploit a network of external collaborations around innovating technologies.

- **Weaknesses and threats:**

The past and current scientific production of LA appears limited and mostly collaborative, leading to a poor national and international visibility. Actions towards the social, economic and cultural environment as well as formation through research are hardly detectable. No plan for corrective actions was presented in the written report. There is currently some inconsistency between expected role of LA and observed lack of interaction with economic environment.

- **Recommendations:**

The sub-critical size of LA needs to be addressed by building a task force adapted to objectives. This probably encourages considering the opportunity to group together unit resources that are involved into the most technological and common parts of projects under a single structure or coordination. The development within the unit of a platform dedicated to directed evolution of microorganisms and generation of synthetic biodiversity is of clear interest and must be reinforced. From a more general point of view, dedicating a team only to applications seems to be a questionable strategy. Most of successful examples enlighten that performance and competitiveness can generally be reached by tightly associating high-level upstream research and application oriented works within the same structure.

Team 7 : Laboratoire de Criblage des Activités de Bioconversions (LCAB)

Name of team leader: Ms Véronique DE BERARDINIS

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	6	5
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	7	6

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		
Theses defended		
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions		1

• Detailed assessments

Assessment of scientific quality and outputs

This group has built a collection of 2594 deletion mutants of *Acinetobacter baylyi* ADP1, for unknown, predicted and known protein functions. For this purpose, they have set up two platforms, one for construction of the complete deletion mutants of *Acinetobacter baylyi* ADP1 and a second one for construction and screening of *Acinetobacter baylyi* ADP1 ORfeome. This collection has allowed them to construct a metabolic model of this bacterium.

Interestingly this team possesses a collection of about 8,000 putative enzymes spanning a range of different families (e.g. aldolases, transketolases, lipases, aminotransferases, nitrilases, alpha-ketoglutarate dependent dioxygenases, Baeyer-Villiger monooxygenases, dehydrogenases, TPP-dependent enzymes etc.). This large collection, which is screened to discover new biocatalysts for specific applications, could also be very useful to improve functional annotation by adding experimental knowledge to the sequence annotation. Since 2008, this group has published 13 papers (2 articles with one LCAB member in the first and/or last position) averaging 2 papers per year, in journals like Mol Syst Biol in 2008, Curr Opin Microbiol in 2009 or more recently Nat Chem Biol in 2014. Indeed co-authorship of a recent paper published in Nature Chemical Biology will help raise the profile of the group.

Assessment of the unit's academic reputation and appeal

The group has only recently been established and hence has only started building its academic reputation. Much of the work currently underway is of high quality and ambitious in nature and if successful will lead to high quality publications which will in turn help to raise the profile of the group internationally. In particular the projects on aldolases and alpha-ketoglutarate dependent dioxygenases should generate novel biocatalysts with interesting synthetic activities. This group has co-organized with LCOB the 24th symposium of the “Club de Bioconversions en Synthèse Organique (CBSO)” in Évry.

Assessment of the unit's interaction with the social, economic and cultural environment

The LCAB team collaborates with LCOB, e.g. together they are currently writing a patent based on the discovery of new reactions catalyzed by dioxygenases. The LCAB/LCOB combination represents an effective way of deriving added value from these two groups in view of their high level of complementarity. The collections of enzymes for new biocatalyst screening were provided to two biotechs (ADISSEO and Global Bioenergies).

Assessment of the unit's organization and life

The LCAB team counts 1 researcher and 6 engineers or technicians but no PhDs or postdoctoral fellows. During the review period, the team has also recruited one master 1 student, two license 3 students and two DUT/BTS students.

Assessment of the unit's involvement in training through research

Currently the LCAB team has no PhD students and hence there is scope to expand this activity to recruit one or two PhD level students. The research carried out in this laboratory is highly suitable for PhD training since a number of the projects have passed the proof-of-principle stage and are poised for further exploitation.

Assessment of the five-year plan and strategy

During the audition, the group leader outlined a clear vision for continuing with existing projects over the next 3-5 years. Indeed, having a wide collection of potential biocatalysts (≈8000) of which approximately 1,500 are experimentally validated and about 300 correspond to purified enzymes, this group now seems to focus more specifically on the characterization of some of the activities with an industrial or pharmaceutical interest. However, they should also consider and build into their 5 year strategic plan the following points: (i) increasing contacts and collaboration with industry; (ii) greater collaboration outside of the unit to raise their international profile; (iii) greater integration with LCOB and LA to form an even more effective grouping.

Conclusion

This group is working in a very topical and important field and is very well placed to really further develop its scientific strategy in the next 5 years. In view of the increasing interest from industry in the application of biocatalysts in the sustainable production of chemicals, the group should seek to expand its horizons and engage more fully with a broader range of stakeholders and funding agencies, including the EU Horizon 2020 program. Consideration should also be given to extending collaborations further to include specialist research groups with expertise in process develop and optimization in order to add further value to the biocatalysts that are being developed.

- **Strengths and opportunities:**

This group has several collections of putative enzymes with potential interest for industrial synthesis operations. In addition, the group has high internal integration potential with both LCOB and LA and together these three laboratories provide a very effective and powerful structure able to span biocatalyst discovery, development, engineering and application.

- **Weaknesses and threats:**

The group is too small to optimally exploit the various resources produced and it seems not to be able to recruit students and postdoctoral fellows. In addition, the perspective for attracting new permanent scientists seems to be low. The international dimension is not visible enough (no european or international funding and not a lot of international communications). The absence of HDR in the team can lead to difficulties in recruiting students. Finally, a low level of interactions with industry was apparent.

- **Recommendations:**

LCAB would benefit from a greater integration with LCOB and LA, particularly in terms of identifying strategic priorities and co-ordinating what are clearly overlapping interests and expertises. The combined expertises would also provide a stronger structure when approaching industry and trying to negotiate collaborations and funding from private sources. The LCAB group is highly encouraged to present their research at international conferences to increase visibility as well as make connections with international peers that could lead to seamless communication and collaboration. Because of the highly competitive nature of this field, the group should still attempt to increase and stabilize its work force by attracting a junior full-time scientist. The committee also recommends that the team leader presents her HDR as soon as possible.

5 • Conduct of the visit

Visit dates:

Start: 16 January 2014, at 9:00

End: 17 January 2014, at 17:00

Visit site:

Institution: Genoscope

Address: 2 rue Gaston Crémieux, Evry

Specific premises visited:

The time allotted to the evaluation committee did not allow any on site-visit, not even a visit to a selected platform.

Conduct or programme of visit:

Day one –16 January 2014	
9:00	Welcome (closed-door) Visiting committee with the AERES Scientific advisor
9:15	AERES representative: the role and procedures of AERES
9:30	Direction of the unit: Past and future, Discussion
10:30	Coffee break
10:45	Team Laboratory of Bioinformatic Analysis for Genomic and Metabolism (LABGeM)
	Talk (past activities, projects) + discussion including the team leader
	Name of the team leader: Ms Claudine MÉDIGUE
11:40	Team Laboratory of genomics and biochemistry of metabolism (LGBM)
	Talk (past activities, projects) + discussion including the team leader
	Name of the team leader: Mr Marcel SALANOUBAT
12:35-12:45	closed meeting
12:45	Lunch
13:30	Team Laboratory of screening of biocatalytic activities (LCAB)
	Talk (past activities, projects) + discussion including the team leader
	Name of the team leader: Ms Véronique DE BERARDINIS
14:25	Team Laboratory of organic chemistry and biocatalysis (LCOB)
	Talk (past activities, projects) + discussion including the team leader
	Name of the team leader: Ms Anne ZAPARUCHA
15:20	Team Laboratory of applications (LA)
	Talk (past activities, projects) + discussion including the team leader
	Name of the team leader: Ms Madeleine BOUZON

16:15-16:30	closed meeting
16:30	Coffee break
16:45	Team Laboratory of metagenomics of prokaryotes (LMP)
	Talk (past activities, projects) + discussion including the team leader
	Name of the team leader: Mr Denis LE PASLIER
17:40-17:45	closed meeting
17:45	Parallel meetings with personnel:
	Discussions with engineers, technicians, administrative
	Discussions with staff scientists
	Discussions with students and post-docs

Day two: 17 January 2014	
8:30	Team Laboratory of bioinformatics sequence analysis (LABIS)
	Talk (past activities, projects) + discussion including the team leader
	Name of the team leader: Mr Patrick WINCKER
9:25-9:30	closed meeting
9:30	Discussion with Doctoral school director
9:45	Discussion with the representatives of the managing bodies
10:15	Discussion with the head of the Center
10:00-17:00	Private meeting of the visiting committee (in presence of the AERES scientific advisor) including lunch
17:00	End of the visit

6 • Supervising bodies' general comments

Evry, le 18 Mars 2014

Michel GUILLARD
Administrateur Provisoire de l'Université d'Evry Val d'Essonne

4, Boulevard François Mitterrand
91025 Evry Cedex

à :

Didier HOUSSIN
Président
Agence d'Evaluation de la Recherche et de l'Enseignement Supérieur
20 rue Vivienne - 75002 PARIS

Réf. AERES : S2PUR150007904

Direction de la Recherche, de la Valorisation et du Transfert

Objet : Réponse au rapport du comité de visite du laboratoire Génomique Métabolique – UMR 8030

Monsieur le Président,

Nous avons pris connaissance avec le plus grand intérêt de votre rapport concernant le projet Génomique Métabolique porté par M. Marcel SALANOUBAT. Nous tenons à remercier l'AERES et le comité pour l'efficacité et la qualité du travail d'analyse qui a été conduit.

Ce rapport a été transmis au directeur du laboratoire qui nous a fait part en retour de ses commentaires que vous trouverez ci-joint.

Nous espérons que ces informations vous permettront de bien finaliser l'évaluation du laboratoire.

Restant à votre disposition pour de plus amples informations, je vous prie de croire, Monsieur le Président, à l'expression de mes salutations respectueuses.

M. Michel GUILLARD

Administrateur Provisoire
de l'Université d'Evry Val d'Essonne

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Génomique métabolique UMR8030

Comments on the report from the visiting AERES committee

16-17 January 2014

Reference number of the report: S2PUR150007904 - GENOMIQUE METABOLIQUE - 0911975C

We thank the visiting committee of the research unit Génomique métabolique (UMR 8030) for their report evaluating our activity and for the useful comments and suggestions. We acknowledge the general conclusions of the report, but think that the scientific history of the unit, i.e. the question of where we come from, must be considered to establish a fair evaluation.

The unit, created in 2000, is hosted by Genoscope and its historical research topics were closely linked to Genoscope's sequencing activity. These activities focused on genome and DNA sequence analysis are still ongoing and as mentioned by the committee maintain their level of productivity and international recognition. This contrasts with the more recent research endeavours. Anticipating on the end of the "golden age of sequencing", the scientific orientation of the UMR was changed drastically in 2005 when the UMR extended its research field to the extensive exploration of enzymatic activities. This represented a dramatic move and required the acquisition of a new culture and know-how. Such a drastic reorientation necessitated also to develop from scratch new scientific tools, to define new long term research goals etc. In a first instance this meant "crossing the desert" before acquiring again credit and visibility the lack of which has been stressed by the committee. In addition, one of our main objectives, the finding of new enzymatic reactions is presently a rather neglected and hence unrewarding field entailing difficulties to find students, post-docs and partners for international projects. We are happy that the visiting committee approves this reorientation and recognizes the importance of this area. In our opinion, the scientific output of the UMR during the last five years can be considered as a real accomplishment.

The presentation of the written report was criticized. Since the possibility to structure the document according to projects or research teams was left open by AERES we choose to submit a document organized by research projects. We naively thought that a presentation of the shared scientific goals, which characterize our main achievements and can best be reached by a strong sense of general interest, was more telling and important for the funding bodies than a display of group-

centered results which remain in many cases only parts of the puzzle. This is perhaps a non-academic view that is closer to a corporate labor-organization, but this reflects the original spirit of Genoscope which has survived in the UMR. In addition when negotiating with private parties, which was so strongly recommended by the committee, it is clear that the shared dedication of multiple groups towards common research objectives is an asset of the unit. We regret that this presentation made the evaluation more difficult for the visiting committee, but it reflects the way we are doing science based on highly collaborative (and interdisciplinary) projects. The committee considers this as a possible weakness/threat for the future. However, we are convinced that our organization is flexible, reactive, encourages “creativity” and “risk-taking” and, because of its large set of expertise, is a strength when tackling new projects. Conversely we share the view of the committee regarding the small size of several teams. There are historical reasons to that, but discussions on a merger of the three smaller teams is in progress and indeed may enhance their overall visibility at the international level.

The interaction with economic partners is judged as very limited by the committee. However we felt that until recently our scientific credibility was not sufficiently established to engage discussions with industrial companies. The situation is changing: a couple of recent publications and oral communications in international conferences have improved our visibility in the field of biocatalysis. With support from the CEA's tech transfer office, negotiations have been entered into with several potential industrial partners, including a large chemical company and a "big pharma". A first MTA (material transfer agreement) was signed early February with an animal feed company and we expect more collaboration to be initiated in the short or medium term. In addition a patent application on dioxygenases has been recently submitted.

A recurrent observation found in this report is the comfortable financial situation of the laboratory. The scientific shift of a large part of the Unit could not have been realized without substantial funding to initiate the high throughput cloning and screening platform that is a unique asset highly appreciated by external collaborators, and the Mass Spectrometry facility which opens up a new way to explore the world of metabolites and their enzymes. Nevertheless we are fully aware of the need of additional external funding (H2020, ERC, industrial contracts, etc) especially for teams involved on experimental science.

Last, we feel that the potentialities of our activities in metabolic engineering and synthetic biology are not sufficiently recognized in the report. If the academic records of the team in charge are probably low, it should be stressed that this team develops innovative concepts of synthetic biology for the exploration of the chemical and metabolic plasticity of living cells. The projects conducted were based on an *in vivo* approach consisting of construction and selection of strains and directed evolution of cell populations through continuous culture. The GM3 automates, thoroughly improved at Genoscope for this purpose, enable the consecutive fixation of adaptive mutations spontaneously appearing in cell suspensions during long term strain adaptation experiments. Microfluidic devices have their advantages but also their drawbacks, notably when selections for rare events require large

populations and hence important volumes. To our knowledge, there is no example of equivalent equipment enabling automated long term chemo- or turbidostat selection experiments; the GM3 devices are rather a competitive advantage for Genoscope and the UMR. The LA team joined the Unit in the second half of 2013 and we think that it will play a driving role in both the conception and the realization of present and future biotechnologically relevant projects of the UMR, notably the implementation of new C1 capture pathways for which the *in vivo* selection and evolution strategy of the laboratory appears to be a promising approach.

I want to thank again the committee for their comments and suggestions. Along with the team leaders and our institutions, we will discuss in a constructive way recommendations suggested by the committee for the next five years.

Marcel Salanoubat
Director of the Unit
« Génomique métabolique »