IAME - Infection, anti-microbien, modélisation, évolution

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on unit:

Infection, Antimicrobials, Modelling, Evolution

IAME

Under the supervision of the following institutions and research bodies:

Université Paris 7 – Denis Diderot

Université Paris 13 – Paris-Nord

Institut National de la Santé Et de la Recherche Médicale

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

Research Units Department

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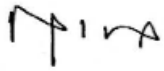


Pierre Glaudes

The president of AERES "signs[...], the evaluation reports, [...]countersigned for each evaluation department by the relevant head of department (Article 9, paragraph 3, of french decree n°2006-1334 dated 3 november 2006, revised).

Grading

Once the visits for the 2012-2013 evaluation campaign had been completed, the chairpersons of the expert committees, who met per disciplinary group, proceeded to attribute a score to the research units in their group (and, when necessary, for these units' in-house teams).
This score (A+, A, B, C) concerned each of the six criteria defined by the AERES.
NN (not-scored) attached to a criteria indicate that this one was not applicable to the particular case of this research unit or this team.

Criterion 1 - C1 : Scientific outputs and quality ;
Criterion 2 - C2 : Academic reputation and appeal ;
Criterion 3 - C3 : Interactions with the social, economic and cultural environment ;
Criterion 4 - C4 : Organisation and life of the institution (or of the team) ;
Criterion 5 - C5 : Involvement in training through research ;
Criterion 6 - C6 : Strategy and five-year plan.

With respect to this score, the research unit concerned by this report (and, when necessary, its in-house teams) received the following grades:

- Grading table of the unit: Infection, Antimicrobien, Modélisation, Evolution - IAME

C1	C2	C3	C4	C5	C6
A+	A+	A+	A+	A+	A+

- Grading table of the team: Quantitative evolutionary microbiology

C1	C2	C3	C4	C5	C6
A+	A+	NN	NN	NN	A+

- Grading table of the team: Ecology, evolution and therapeutic of virulence and resistance in bacteria

C1	C2	C3	C4	C5	C6
A+	A	A+	A+	A+	A

- Grading table of the team: Antiretroviral resistance, genetic diversity and therapeutic strategies in HIV infections

C1	C2	C3	C4	C5	C6
A+	A	A+	A+	A+	A+

- Grading table of the team: Biostatistical modelling, pharmacometrics and clinical investigation in infectious diseases

C1	C2	C3	C4	C5	C6
A+	A	A+	A+	A+	A+

- Grading table of the team: Decision sciences in infectious disease prevention, control and care

C1	C2	C3	C4	C5	C6
A+	A	A+	NN	A+	A+

Evaluation report

Unit name:	Infection, Antimicrobials, Modelling, Evolution
Unit acronym:	IAME
Label requested:	INSERM
Present no.:	
Name of Director (2012-2013):	Mr Erick DENAMUR
Name of Project Leader (2014-2018):	Mr Erick DENAMUR

Expert committee members

Chair:	Mr Didier MAZEL, Institut Pasteur
Experts:	Mr Bonaventura CLOTET, University of Barcelona, Spain
	Mr Ulrich DOBRINDT, University of Münster, Germany
	Mr Paddy FARRINGTON, University of Milton Keynes, UK
	Mr Bernard LA SCOLA, University of Marseille, (CNU representative)
	Mr Csaba PAL, University of Szeged, Hungary
	Ms Marie-Cécile PLOY, University of Limoges, (INSERM representative)
	Ms Valérie SEROR, University of Marseille
	Mr Philippe VANHEMS, University of Lyon

Scientific delegate representing the AERES:

Ms Sophie DE BENTZMANN

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

Ms Christine CLERICI, Paris 7 University

Ms Laurence LOMME, INSERM

Mr Jean Loup SALZMMAN, Paris 13 University

1 • Introduction

History and geographical location of the unit

The future Unit, and its 5 teams, will be located in the Hospital Bichat /Paris Diderot University Campus, Paris 75018, mostly in the University building. The proposed IAME unit gathers two former Inserm units, the UMR-S 722 and 738, which were respectively led by Mr Eric Denamur and Ms France Mentré, who will be the chair and deputy chair of the new structure, respectively. IAME also integrates 3 former "Equipes d'Accueil" of the faculté de médecine and the Équipe ATIP/Avenir of Mr Yazdan Yazdanpanah. Team 1 is a new team led by a young PI, who was previously developing his project inside the Denamur team in Inserm unit-S 722, and who was recently awarded an ERC grant. These five teams share a common interest for the understanding of the ecological and evolutionary forces that allow microorganisms (bacteria and viruses) to adapt, become virulent and resistant to antimicrobial therapies. The 5 teams will focus on three classes of organisms for which they have strong and internationally recognized expertises: multiresistant enterobacteria, HIV and HCV. Many scientists involved in the projects are medical doctors with clinical practice, and they have numerous connections with hospital services, which can be seen as promising for the translational projects they propose. They already have a long history of collaborative work, and their project clearly reflects their strong will to strengthen and expand further their collaboration and develop new projects at the interface of their different domains.

Management team

The IAME unit will be chaired by Mr Erick Denamur, and Ms France Mentré, as deputy chair. The administrative direction will be delegated to an administrative manager. A unit council, gathering the 5 teams directors and the administrative director, will meet on a regular basis. A hygiene and safety team is already created. A common funding model is proposed, where 10% of the operating grant will be shared by the whole unit. Yearly unit retreats of 1.5 days are scheduled, as well as seminars with external invited speakers. In order to expand inside collaboration and knowledge sharing, several scientific clubs will be organized with meeting on regular basis.

AERES nomenclature

SVE1_LS2, SVE1_LS7, SVE1_LS8

Unit workforce

Unit workforce	**Number as at 30/06/2012**	**Number as at 01/01/2014**	2014-2018 **Number of project producers**
N1: Permanent professors and similar positions	21 (8.25)	26 (10)	21 (8.25)
N2: Permanent researchers from Institutions and similar positions	18 (7.7)	21 (9.1)	18 (7.7)
N3: Other permanent staff (without research duties)	7 (4.95)	6 (4.45)	3 (2.8)
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)			
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	10 (6.2)	15 (9.2)	10 (6.2)
N6: Other contractual staff (without research duties)	2 (1.5)	4 (3.5)	
TOTAL N1 to N6	58 (28.6)	72 (36.25)	52 (24.95)

Percentage of producers	*100%*

Unit workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	27	
Theses defended	23	
Postdoctoral students having spent at least 12 months in the unit*	5	
Number of Research Supervisor Qualifications (HDR) taken	6	
Qualified research supervisors (with an HDR) or similar positions	27	31

2 • Assessment of the unit

Globally, the research carried out at the Unit can be qualified as excellent.

Strengths and opportunities

The Unit will be clearly visible in the French and international research landscape, as each of its team is already internationally recognized in its field. The gathering of the 5 teams offers a unique opportunity to create a synergy between these teams and develop a true promising translational program from basic research on evolutionary mechanisms and models in bacteria and viruses and on the way they may evade treatment strategies, to statistic modelling and assessment of health policy. The structure will also offer a single entry to this impressive consortium, and will guarantee a much higher visibility for their research. A convincing effort has been made to build on the different expertises, even inside the largest team. They already have an impressive collaborative past, with 132 publications involving at least 2 of the 5 teams in the past 5 years.

This Unit provides a prime example of the value of an association between INSERM, Hospital and University by providing excellence in research, teaching, and training of MD / PhD students. They trained 23 PhD during the last period and 27 are still to be defended. They published a lot in both clinical and basic science peer reviewed journals, and were able to place their major contributions in top ranked journals (Science, Nature Medicine, PLoS Biology, PLoS Genetics, PLoS Pathogens, Lancet, NEJM, JAMA, PNAS USA, etc.). The 5 different teams have been able to forge excellent collaborations, national and international, giving them access to cutting-edge technologies and/or knowledge.

They have been able to raise excellent funding, from National agencies, but also from European calls.

Weaknesses and threats

Only few were identified. Three concerns have been raised by the committee, which were also identified as such by the unit staff. The first is the limited number of full time scientists in most teams. This can be a serious problem for several of these teams, where the present workload is big and certain expertises only carried by a single researcher within a given team. This is also true for the rather limited number of technicians and engineers (especially for computing and statistics).

The second weakness is the current lack of attractiveness for foreign students and postdoctorants even if the different teams have good connections with excellent foreign labs. This is certainly due to the low visibility of the former small units, and hopefully the current organisation scheme, with the regrouping of these different teams, will provide better visibility. Finally, as many projects rely on mathematics, statistics and evolutionary biology, it is very important to develop relationships with either engineer schools or university in these fields, to insure a constant influx of students in these fields.

As for any research unit, even if extremely successful over the last period, funding is also an issue, especially with the current lack of vision of the next European program and of its priorities. The unit recurrent funding from Inserm, and from universities Paris Diderot and Paris Nord is reasonable, but cannot support the ambitious projects of the different teams.

Recommendations

The very strength of the IAME unit project is its integration, from evolutionary biology, molecular biology, bacteriology, virology, modelling, to risk assessment and health policy decision. This is unique and very promising, but relies on the cohesion of the different teams, which would “feed” each other. The management of the unit should maintain its effort to guarantee the cohesion of the unit by ensuring regular meetings involving the scientists of the different teams under the form of the proposed thematic clubs, or by any other means. In this line, gathering the different teams of the IAME unit in a single location on the Bichat campus would reinforce the cohesion of the unit and favour collaborations and exchanges. From the practical point of view, it is very important to create an in house L3 laboratory, to handle highly pathogenic microbes. The specific evaluation of individual team projects only suggests a few minor adjustments, mostly dealing with a couple of subprojects that have not been considered not as ambitious and promising as the others, especially in this “hospitalo-universitaire” context, where most permanent staff are only part time researchers.

3 • Detailed assessments

Assessment of scientific quality and outputs

The relevance and the originality of research conducted is attested by the excellent scientific records of the 5 teams, and the research they carry on has a strong echo in the community. This is true for the peer-reviewed articles published by all teams, but also for the softwares developped and distributed by team 4. They produced more than 700 publications, in both clinical and basic science journals, among which more than 20 in top ranked journals (Science, Nature Medicine, PLoS Biology, PLoS Genetics, PLoS Pathogens, Lancet, NEJM, JAMA, PNAS USA, …). The 5 team leaders are all internationally recognized leaders in their field, and are invited speakers in international conferences in their fields, on a regular basis.

Assessment of the unit's academic reputation and appeal

The academic reputation of the different teams is excellent, this is reflected by their success in application at both national and international levels, and the invitations they got to give lectures in international conferences. At the national level, their attractivity is obvious, however, this is one of the few identified weaknesses, they so far mostly attracted French students and postdoctorants. The ERC banner should help improve this situation. As medical school based unit, they attract a lot of MD students. They are members of different national and international networks.

The high academic reputation of the Unit is also mirrored by the participation of the PIs in scientific committees and advisory boards of funding agencies in France (Fondation pour la Recherche Médicale, Scientific Council of the Université Paris Diderot, Scientific Committee of the ANR “Accompagnement Spécifique des Travaux de Recherches et d’Innovation Défense).

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

The different teams are all engaged in actions beyond their academic environment. They are involved in teaching in different universities and Engineer schools, they have contributed to a wide ranging of teaching initiatives and teaching materials, Team 4 has invested time and effort into developing their PFIM, SAEMIX, NPDE software tools, which have been made freely available to the academic community as R packages, or have been incorporated in existing packages. PIs have been involved as advisors in different scientific councils (Fondation pour la Recheche Médicale, Haut Conseil de Santé Publique, …). They actively investigate scientific questions which are of great interest for improvement of diagnostic, preventive and therapeutic approaches supporting the quality of life and public health. They have good connections with the pharmaceutical industry at different levels, and filled in several patents. The only exception is Team 5, which has no interactions with pharmaceutical industry, but this is obviously a prerequisite to make independent economic assessments. On the other hand, they have many interactions with national and international health decision agencies.

Assessment of the unit's organisation and life

The unit organization is simple and efficient, with a Unit council. The council will gather the heads of the different teams and the administrative director, and will meet twice a year, or more when necessary. This council will take all urgent decisions and make adjustments. They propose to have a scientific retreat for the whole unit for 2 days once a year, while each team will have weekly lab meetings. An agreement has been made for the sharing of 10% of the operating grants. From the discussions with the different staff categories (Researchers, ITAs (technicians /engineers /administrative) and students/postdocs), everyone seems to be happy with the organization, with a few minor points reported such as a need for an uniformized access to training plans (“formation continue”), or the rather low number of technicians for such a large unit. The relevance of initiatives aimed at reinforcing the cohesion and the interactions between the different teams, emergence of cutting edge projects and taking of risks are good, with the few readjustments detailed in the teams reports. The involvement of the unit’s members in teaching activities and in clinical pratice at the local level is a characteristic of the Unit, with most staff scientists involved in teaching duties in different university and medical school programs.

Assessment of the unit's involvement in training through research

The different teams trained 23 PhD students during the period of evaluation and there are currently ongoing 27 PhD students. As mentioned above, PIs and staff scientists are all involved in teaching both for medical students and master students.

Assessment of the five-year plan and strategy

All the projects are originals, ambitious, timed and propose integrated approaches. All proposed projects are relevant and feasible, with a few minor readjustments. Among the projects, several are risk-taking but this is clearly justified and should be rewarding.

4 • Team-by-team analysis

Team 1 : Quantitative evolutionary microbiology

Name of team leader: Mr Olivier TENAILLON

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1 (0,35)	2 (0,70)	1 (0,35)
N2: Permanent EPST or EPIC researchers and similar positions	2 (1,5)	3 (2,5)	2 (1,5)
N3: Other permanent staff (without research duties)	1 (0,8)	1 (0,8)	1 (0,8)
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3 (1,85)	5 (3,85)	3 (1,85)
N6: Other contractual staff (without research duties)		2 (2)	
TOTAL N1 to N6	7 (4,5)	13 (9,85)	7 (4,5)

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	1	
Theses defended (2009-2012)	5	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

Team 1 is a new team with huge potential. The leader of the team has already proved his scientific charisma on several occasions. In the last five years, he has published several exciting papers that have reached top-ranked journals (2 PNAS, 1 Science, 1 Plos Genetics) and generated broad interest from the scientific community. Most notably, the team leader is the first author of a recent work in Science. It is a very important and thought provoking paper. For the first time, it integrates high-throughput experimental evolution and genome sequence analyses to gain a better insight on evolutionary convergence. The team leader has also recently received the prestigious ERC starting grant. This grant is a major boost for developing lab infrastructure and to perform high-throughput analyses.

Assessment of the unit's academic reputation and appeal

The principal investigator (PI) is a world-renowned expert on bacterial evolution. The team's interest is very broad, and integrates approaches of many related fields (including microbiology, experimental evolution and population genetics). In the emerging field of evolutionary system biology, combining these techniques is the key to reach outstanding results with potential practical implications. The team collaborates with several outstanding scientists around the globe. The PI has been invited as speaker to numerous prestigious scientific events, and is a regular reviewer for top-ranked scientific journals and scientific agencies. The PI is a reviewing editor for Journal of Evolutionary Biology.

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

The projects initiated by team 1 could potentially generate public interest. Analyses of human microbiota, and evolution of antibiotic resistance in microbes are important topics with obvious medical implications. The team is well embedded into infrastructure of the campus, and has several outstanding in-house collaborations with other teams in the unit.

Assessment of the unit's organisation and life

The team plans to hold regular meetings and seminars. Given the multidisciplinary nature of the lab, PhD students will have excellent opportunities to learn a wide range of techniques, scientific concepts and compare the approaches.

Assessment of the unit's involvement in training through research

Non applicable, team 1 has only very recently been established.

Assessment of the five-year plan and strategy

Overall, the proposed projects are very impressive and innovative. The team seeks to construct and validate experimentally models of microbial adaptation. The team will combine top down (phenomenological) and bottom-up mechanistical approaches. They will investigate several key issues in evolutionary biology including a) the constraints on protein evolution, b) phenotypic complexity, c) prevalence and mechanisms of epistasis, and d) microbial diversity and evolution in the gut. Although the canvas is vast, all subprojects are feasible. Subproject 1 is concerned with the evolution of TEM1 protein. It combines high-throughput mutational and phenotypic analysis of this protein with computational protocols that estimate protein stability and other thermodynamic properties. The idea to compare experimental results with simple biophysical model is intriguing. Subproject 2 aims to analyse phenotypic complexity with the aid of computational models of metabolic network and simple molecular analyses. For the first time, the team will investigate the conditions that favour specific gene regulatory modes. In subproject 3, the team will investigate long-term experimental evolution of E. coli in mouse gut. While this idea is novel and exciting, it may be difficult to interpret the outcome. For example, changing host diet may have a direct effect on the evolutionary pressure on E. coli or modify the abundance of competitor bacteria. Subproject 4 is part of a large project on twin genome wide association and microbiota studies.

Conclusion

- Strengths and opportunities:

The PI of team 1 has made outstanding contributions to a wide range of topics on microbial evolution. As a recognition of these achievements, the team has gained substantial support from the European Research Council. Integrating computational biology with microbial laboratory evolution experiments and functional genomics will provide an unprecedented opportunity to reach major breakthroughs in this field.

- Weaknesses and threats:

The projects are only weakly linked to each other, and very diverse. Given that team 1 has only recently been established, the principal investigator will probably have many extra duties with recruiting scientists, negociating with lab equipment selling companies, and improving cohesion.

- Recommendations:

Recruiting skilled senior scientists and technicians will be very important for successful realization of these ambitious projects. The team website needs much improvement. It should give more detailed and updated information on research interest, ongoing projects, publications, details of lab members with contacts.

Team 2 : Ecology, evolution and therapeutic of virulence and resistance in bacteria

Name of team leader: Mr Erick DENAMUR

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	13 (5)	14 (5,35)	13 (5)
N2: Permanent EPST or EPIC researchers and similar positions	8 (2,9)	8 (2,9)	8 (2,9)
N3: Other permanent staff (without research duties)	3 (3)	3 (3)	2 (2)
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	3 (1,5)	4 (2)	3 (1,5)
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	27 (12,4)	29 (13,25)	26 (11,4)

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	10	
Theses defended (2009-2012)	10	
Postdoctoral students having spent at least 12 months in the unit	0	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	18	19

• Detailed assessments

Assessment of scientific quality and outputs

Team 2 represents an internationally highly renowned and scientifically active interdisciplinary research team with signifcant scientific output of excellent quality. The team focuses on Escherichia coli as a model system to study bacterial evolution, population genomics and diversity with implications on bacterial virulence, commensalism and adaptation. In the last five years, the team leader has been co-author/senior author on 44 publications in peer-reviewed journals with high scientific reputation including several papers in leading and high-impact journals (Science, PLoS Genetics, PLoS Pathogens). The PLoS Genetics corner-stone paper on E. coli genome plasticity and adaptation has even been cited 209 times since it has been published in 2009 (average citations per year: 41.8; Thomson Reuters Web of Science).

Assessment of the unit's academic reputation and appeal

Team 2 has a high academic reputation and is nationally and internationally well-recognized. The principal investigators (PIs) of the unit have been involved in the organization of multiple national and international conferences in France and elsewhere. Furthermore, they have been invited as speakers at scientific seminars/symposia of Universities in France, European or other countries. The high academic reputation of the team is also mirrored by the participation of the PIs in scientific committees and advisory boards of funding agencies in France (Fondation pour la Recherche Médicale, Scientific Council of the Université Paris Diderot, Scientific Committee of the ANR “Accompagnement Spécifique des Travaux de Recherches et d’Innovation Défense”) as well of different journals. Documented interactions exist with leading teams worldwide regarding E. coli population genetics. There are also documented interactions with well-known researchers and PIs of other research institutions/universities in Paris.

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

Further research grants were successfully received from French and other funding sources. Some of these grants were preferentially meant for promoting young scientists (ANR Jeune Chercheur) or strengthening of international cooperations (Centre de Coopération Universitaire Franco-Bavarois). The contribution of the team leader to educational programs of the French Ministry of Education regarding teaching and education guidelines for high school teachers mirrors his engagement beyond his own academic environment. Furthermore, the team actively investigates scientific questions which are of great interest for improvement of diagnostic, preventive and therapeutic approaches supporting the quality of life and public health. The scientific output of team 2 is also of interest for the pharmaceutical industry (patents have been filed).

Assessment of the unit's organisation and life

The unit’s organization follows generally acknowledged principles of good scientific and laboratory practice. The leadership is greatly appreciated and respected in the entire team. General meetings are held regularly. Operational safety measures seem to be effective. A website is maintained and provides information/communication of results for internal and external visitiors. The team is embedded into the framework and infrastructure of the Bichat campus.

Assessment of the unit's involvement in training through research

The team combines research and education: 11 PhD students have been trained in the last five years. The team is regularly involved in teaching of PhD and MD students at different levels as well as in the practical education of undergraduate students.

Assessment of the five-year plan and strategy

Fundamental research on E. coli diversification and adaptation: The general question in the research focus of Team 2 is to understand adaptation and diversification of *E. coli*. The team analyzed metabolic traits to determine whether different *E. coli* pathotypes and lifestyles can be correlated with individual metabolic properties. As one of the first groups worldwide, Team 2 applied whole-genome sequencing as the method of choice to address this question. Complete Escherichia genome sequences were analyzed with regard to genome content and the composition/size of the core- and pangenome. The core genome has been defined to contain app. 2000 genes, whereas the pangenome seems to comprise 10 time more genes. These data further underline the significant genome plasticity of *E. coli*. The genome content analysis of extraintestinal pathogenic *E. coli* added to results of other research teams worldwide, that ExPEC cannot be characterized on the basis of one set of virulence markers and a uniform infection strategy, rather ExPEC infection is a multifactorial process. Genome plasticity is not restricted to the transfer of relatively small genomic regions, but can also involve horizontal transfer of large genomic stretches (incl. mobile DNA elements AND the chromosomal backbone) by conjugation. Metabolic diversity of different *E. coli* subgroups and phylogenetic lineages has been analyzed and combined with results from the whole genome sequence analysis. Interestingly, although lineages with different genetic background or lifestyle can be predicted, the analysis of metabolic networks based on complete genome sequence information indicated that such defined lineages do not exhibit specific metabolic profiles and that phenotypic diversity of *E. coli* involves rather regulatory differences than differences in gene content. Nevertheless, studies on gene expression and enzyme activities upon cultivation under different growth conditions suggests that specific metabolic activites can support individual liefstyles, e.g. that of uropathogenic *E. coli*, because metabolic acitivities and stress response can protect and support colonization of *E. coli* in the specific niche (e.g. the urinary tract). The impact of components of the flexible gene pool to pathogenicity and fitness has been assessed in different experimental infection models including rats and several surrogate hosts. Interestingly, the results have been interpreted in a way that extraintestinal virulence is a by-product of commensalism as "virulence traits" contribute to fitness in the intestinal tract.

E. coli **epidemiology:** Other research activities with a more epidemiological focus included the analysis of a possible link between epidemiology and virulence/niche adaptation.Team 2 worked on *E. coli* septicemia isolates and analyzed whether their gene content could be correlated with severity of disease. Their interesting results imply that host factors and portal of entry are more important for the outcome of the disease than bacterial virulence gene content. Nevertheless, certain antibiotic-resistant lineages are more virulent than their sensitive relatives. Furthermore, their results show that virulence data obtained from experimental animal infection models of septicemia may not be representative for the human situation. Another study showed that the oropharynx and trachea of intensive care unit patients can be colonized by *E. coli* strains that belong to their own fecal flora. The group also characterized genome content, fitness and virulence traits of a currently successfully spreading pandemic ESBL-producing *E. coli* clone (O25b, ST131).

With their portfolio of expertises, Team 2 complemented their work on pathogenic *E. coli* by epidemiological analyses on (i) environmental or non-mammal commensal isolates, (ii) human and animal commensal isolates from indigenous Amerindians in French Guayana, or (iii) isolates from secondary habitats such as water and sediments. These environmental and commensal isolates were shown to differ with regard to population structure, virulence, antibiotic resistance, fitness and general growth abilities from human isolates. Furthermore, a human-specific clone of phylogenetic lineage B2 has been identified and its capacity to be used as a probiotic has been evaluated (a patent has been deposited).

Based on the previous research activities, Team 2 has a large fundus of thoroughly collected and well-characterized *E. coli* isolates from defined environments or patient groups as well as a significant background and expertise regarding analyses on population structure, geno- and phenotypic diversity and pathology of *E. coli*. In the next five years Team 2 plans to:

1) further extend these collections from different natural environments, different human subpopulations or different groups of patients,
2) analyze the population structure and genomic variability of these isolates to study ecological and genetic factors involved in specialization/adaptation to different growth environments,
3) characterize in detail adaptational strategies and mechanisms on the molecular level in order to correlate genomic alterations and altered protein functions with specific niche adaptation or the transition from non-pathogenic to pathogenic *E. coli* variants,
4) study conditions which promote the spread of antibiotic resistance in *E. coli* (reservoir of resistance determinants, horizontal gene transfer, impact of resistance determinants on bacterial fitness),

5) develop new or improved approaches for antibacterial therapy (phage therapy, probiotics) to treat ExPEC infections, especially those caused by ESBL producing *E. coli*.

This integrated approach addresses very timely and important questions contributing not only to increased scientific knowledge, but also to an improved quality of life. The expertise of Team 2 ensures that significant and relevant achievements will be made.

Conclusion

● Strengths and opportunities:

One unique feature of Team 2 is the integrated genome wide analysis of pathogenic and commensal *E. coli*, i.e. the combination of next-generation sequencing (NGS) data with phenotypic analyses (investigation of metabolism, stress response), functional genomic and epidemiological studies. This goes beyond frequently performed investigations focusing only on either genome content or phenotypes. Team 2 is one of the few teams worldwide, and the only team in France and Europe, with high visibility, excellent reputation and expertise in this field, also being a "motor of innovation" for this type of analysis. At the moment,Team 2 is probably the only team worldwide that is successfully performing this integrated approach on a large-scale.

The team combines relevant research topics of fundamental general microbiology and clinical microbiology. Problems in clinical microbiology are systematically addressed by fundamental multidisciplinary research approaches. The team addresses timely and important threats regarding health care and treatment in industrialized countries: *E. coli* infection of different body niches (urinary tract, bacteraemia, ventilator-associated pneumonia, diarrhea), spread of highly pathogenic, multi-resistant clones; evolution of pathogenic bacterial variants, prevention/treatment of ESBL infection and resistance development.

A unique *E. coli* strain collection has been established which is also of great interest for other researchers. This collection should be integrated in the hospital/university center for biologial ressources.

● Weaknesses and threats:

The proposed work plan is very ambitious and includes quite diverse subprojects, all of which are centered around different aspects of *E. coli* commensalism and pathogenicity. These single projects could, however, also be independent projects on their own and therefore strong integrative efforts should be made to avoid mere co-existence of the different sub-teams. A significant part of the workplan is devoted to relatively descriptive analyses of, e.g. population structures, metabolic activites, etc. This is, without doubt, very important. Nevertheless, these studies will have even greater impact if they can be combined with detailed molecular studies to characterize the underlying mechanistic aspects.

The proposed workplan will result in the generation of a vast amount of data. Sufficient informatics infrastructure and manpower (mathematicians, bioinformaticians) will be needed to analyse and process these data so that they will also be beneficial for further analyses (eventhough strong connections exist with team 1, which was previously part of the team).

Certain parts of the analysis of spread of ESBL plasmids should be reconsidered. The combination of, e.g. research on the spread of ESBL plasmids among *E. coli* and gonococci is less convincing.

● Recommendations:

To further improve national and international visibility, it could be recommended to concentrate on internationally competitive and highly visible fields of expertise of this team. The real strengths and core competences should be promoted. Complementation of the more global, descriptive studies with detailed mechanistic analyses will increase the impact of the results.

The team should take advantage of the complementary expertise of the different subteams and make strong efforts to carefully integrate the different subtasks. Only by this an additional value will be achieved.

Further support and strengthen activities regarding modelling and bioinformatic analysis of data obtained from (meta-)genomic, metabolomic and population genomic analyses have to be found.

Team 3 : Antiretroviral resistance, genetic diversity and therapeutic strategies in HIV infections

Name of team leader: Ms Diane DESCAMPS

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	3 (1.2)	4 (1.55)	3 (1.2)
N2: Permanent EPST or EPIC researchers and similar positions	4 (0.6)	4 (0.6)	4 (0.6)
N3: Other permanent staff (without research duties)	1 (0.15)	1 (0.15)	0
N4: Other professors (PREM, ECC, etc.)	0	0	0
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1 (0.35)	2 (0.5)	1 (0.35)
N6: Other contractual staff (without research duties)	1 (1)	1 (1)	0
TOTAL N1 to N6	10 (3.3)	12 (3.8)	8 (2.15)

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	2	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	0	
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs

The team leader is an internationally recognized expert in the field of HIV resistance. Globally the research carried out by the team should be qualified as excellent, especially taking into consideration that HIV resistance is a highly competitive field. The team leader is co-author/senior author on more than 70 publications in peer-reviewed journals for the period, several papers are published in leading journals (Clinical infectious diseases, PLoS Pathogens, J. Antimicrob. Chemotherapy, AIDS …) and have achieved high citation index. Her papers have been very useful for setting up very valid rules for a proper clinical management of resistance to anti HIV drugs.

Assessment of the unit's academic reputation and appeal

This team is one of top leaders in the world on HIV resistance and treatment strategies. It hosted the CNR for HIV resistance which has been extended for the next 4 years. The team has been implicated in the coordination of the International Achieve HIV-2 network.

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

The research themes of this team fit perfectly with the clinical and social environment of its academic center (many infected patients followed by the academic hospital).

Assessment of the unit's organisation and life

The team is well organized with very regular research meetings sharing through the researchers all the results and the new program designs. All the researchers have the opportunity to attend international research meetings to present themselves their results, as it is attested by their publications and communications.

Assessment of the unit's involvement in training through research

The members of the team are deeply involved in teaching in masters and PhD research programs: Pasteur Institute, Universities of Science and Medicine. The unit is training two doctoral and one post doctoral students.

Assessment of the five-year plan and strategy

The 5 year plan is very interesting and promising. A diversification of the topics has been planned (Reservoir studies and drug discovery) showing that the team leader has anticipated the evolution of the research in HIV/AIDS field. In order to cope with all goals, the team leader should get more support for incorporating more people involved in research.

Conclusion

● Strengths and opportunities:

An evident strength is the successful research conducted by the team leader during the last 18 years. She has shown an enormous capability to adapt to a very evolving and challenging field. Definitely, she has consolidated her research. The team leader has focused on the different resistance profiles emerging with the different ant iHIV drugs becoming available through time. Furthermore the team has characterized polymorphisms in the different HIV subtypes and its association with resistance to different drugs. The team has pointed towards a translational research with clear clinical applications. The team has adapted to the evolving field even when it has moved to a more sophisticated area represented by the minority variants and its clinical significance. The team has contributed significantly looking at the gag-pol minority variants and its association to protease inhibitors resistance.

The results obtained have been very important for building the resistance guidelines for HIV-1 and HIV-2 used in France for a proper use of anti-HIV therapy. Indeed these guidelines have also been widely recommended abroad. The studies on molecular determinants of HIV-2 R5-X4 tropism in the V3 loop have permitted the development of a new genotypic tool. The team has also focused on the survey of resistance in naïve patients in developing countries. This is extremely useful and important in order to define the most adequate first line therapy. The team has now the opportunity to define more precisely the role of minority variants, mostly in experienced patients but at all lines of treatment failure (from first line to rescue approaches) both in HIV-1 and HIV-2 and also in different HIV-1 subtypes. Also through all the survey studies in Africa, the team work could continue being of great importance for guiding properly the use of ARVs for HIV-1 in poor resource countries. Also by focusing on HIV-2, the team could contribute significantly to the understanding of the resistance profile emerging to this virus for all upcoming drugs targeting specifically HIV-2. This will be very important in Africa but also in the rest of the world where HIV-2 could become more prevalent in the future through immigrants that carry the virus when moving to other countries. The tema knowledge about the molecular mechanisms of resistance could provide insights for designing new antiretrovirals with higher potency in case of resistance or with a higher genetic barrier to resistance.

- Weaknesses and threats:

A major threat lies in the current and future limited funding specially for anti-HIV resistance studies and tropism assessment through genotype. These topics have been significantly funded in the past (i.e., CHAIN project WP7 EU in which the team leader is currently involved but that will finish in 2014). No more grants can be expected from EU for resistance analysis, tropism, role of minority variants or surveillance. However, in France, it seems that INSERM/ANRS has re-conducted its effort to fund research about resistance to antiretrovirals (that was one of the most productive topic in ANRS) in developed and developing countries and the team leader is now coordinating the INSERM/ANRS resistance study group. The team is also moving to diversify the activity of research in two new directions: exploring new fields of HIV-2 infection (accessory genes and characterization of reservoir) and anti HIV-2 drug design.

The team is small and for all the goals she has for the future, there is a need to increase the number of doctoral / post doctoral students, mostly considering her interest on these new topics: pathogenesis specifically focused on HIV-2 (characterization and quantification of HIV-2 reservoir, role of accessory genes) and in new drug discovery, through *in silico* analyses, including comparison of drug binding sites on HIV molecules, simulation of interactions and virtual screening approaches. The team should set up a close collaboration with other groups working in the assessment of the reservoir in HIV-1 infected people.

Also a frequent problem for staff-members results from the heavy teaching load that they must assume.

- Recommendations:

To reach their planned research-goals regarding resistance to HIV-1 and HIV-2 and viral tropism they have to consider, as mentioned before, that in 2014 ends the financial support coming from the CHAIN grant and that most probably no other source of money from European Organisms are expected to come out for application in these fields.

However, the fact that the team leader is now the leader of the resistance study group of INSERM/ANRS will probably allow her to secure funding through this agency.

Because their area of expertise has been so far mainly focused on resistance they need to move to other areas where funding could become more available. Eradication is one of the new “hot topics” in HIV research and they have very properly selected it for research. What is also remarkable is their choice of HIV-2, which could provide very interesting findings applicable hopefully also to HIV-1 eradication. Most of the groups focus only in HIV-1 but there is a a need also to generate information about HIV-2. The innovation in drug discovery seems also very interesting mostly if it is also focused on HIV-2. If possible regarding this virus (HIV-2), it could be of interest to train physicians from Africa. This topic has been considered by INSERM/ANRS as a priority and the team leader will be involved in 2013 as a new group dedicated to antiviral discovery. This area has a major interest for producing real innovation, creating interactions with very different departments allowing high level innovative research (Medicine departments associated with Chemistry, biomathematics departments, etc.).

Team 4 : Biostatistical modelling, pharmacometrics and clinical investigation in infectious diseases

Name of team leader: Ms France MENTRÉ

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	3 (1.2)	3 (1.2)	3 (1.2)
N2: Permanent EPST or EPIC researchers and similar positions	2 (1.2)	2 (1.2)	2 (1.2)
N3: Other permanent staff (without research duties)	2 (1.0)	1 (0.5)	
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1 (0.5)	1 (0.5)	1 (0.5)
N6: Other contractual staff (without research duties)	1 (0.5)	1 (0.5)	
TOTAL N1 to N6	9 (4.4)	8 (3.9)	6 (2.9)

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	10	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	4	4

• Detailed assessments

Assessment of scientific quality and outputs

The research undertaken is very diverse, and spans a broad scientific spectrum from biostatistics to clinical medicine. In biostatistics, the team has made an outstanding contribution to the emergence of pharmacometrics as a subdiscipline of clinical pharmacology. The importance of their work on nonlinear mixed effects models transcends the application area on which they have focused, namely pharmacokinetic and pharmacodynamic modelling, and has wider application in many branches of statistical epidemiology and beyond. Their work on optimal design, model evaluation and diagnostics has found direct application in pharmaceutical research, and has led to fruitful international collaborations. The team's clinical research has made important advances in the study of treatments for HIV and influenza, both with important impact on clinical practice and public health.

The outputs achieved by the team are excellent in their quantity, quality and diversity. The large number of peer-reviewed papers published (and currently in press) over the 2007 – 2012 period by what is really quite a small core team of researchers is extremely impressive. The team's publications are very diverse, spanning several disciplines and sub-disciplines, reflecting the breadth of the team's mutidisciplinary approach. There are many publications in top international journals with exacting quality standards. For example, the team has published papers in leading statistics journals, such as *Biostatistics*, *Biometrics*, *Statistics in Medicine*, *Journal of Statistical Planning and Inference*; world-class general medical journals such as *Nature Medicine* and *The Lancet*; top international specialist medical journals in a very wide variety of medical fields, such as *AIDS*, *Vaccine*, *Journal of Infectious Diseases*, *Heart*, *Stroke*, *Circulation* to name but a few. Team members are well represented as key authors on these publications. Members of the team have been very active on the national and international conference circuit, given large numbers of presentations or posters, both invited and contributed, at a very wide range of meetings. An added value is the close relationships with the clinical teams, inside the team but also outside because of a strong involvement in hospital activities. This facilitates interactions with clinicians and biologists, but also places Team 4 in a favourable context for tackling emerging clinical research questions.

Assessment of the unit's academic reputation and appeal

The team comprises several researchers with world-class reputations in their respective domains. This, together with the team's sustained high quality outputs, has ensured a high degree of academic visibility. Thus, over the review period, team members received no fewer than 25 invitations to present their work at international conferences and workshops. The team leader has been invited to organise special sessions at both the International Biometric Conference and the annual conference of the International Society for Clinical Biostatistics. The team has several national and international collaborations, with researchers in the UK, Sweden, Switzerland…. The group is a partner of in a FP7 Innovative Medicine Initiative European collaboration, and, jointly with researchers at London University, initiated an annual cycle of international workshops on optimal design of experiments. The team has external funding from French research agencies.

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

A most impressive and commendable achievement is the team's success in translating methodological development to software implementation, notably their PFIM, SAEMIX, NPDE software. The team has invested time and effort into developing such software tools. These have been made freely available to the academic community as R packages, or have been incorporated in existing packages. In this connection, there is a productive research and development relationship with several industrial partners from the pharmaceutical industry, notably Sanofi, Servier, Novartis, and Roche. This is a distinctive and outstanding feature of the team's work which should be maintained in future, and valorised appropriately. Within the academic community, team members have been active in organising conferences and conference sessions. Members of the team have been invited to join the editorial boards of three international journals. Within the social sphere, one team member has been appointed as an expert at the Haut Conseil de Santé Publique, and others have provided expertise in academic, industrial and public health contexts. As for teaching, the Unit has a sustained involvement at Master level, and coordinates an Inter-University Diploma on anti-microbial use. Team members have contributed to a wide ranging of teaching initiatives and teaching materials. Overall, it is clear that the team has a sustained engagement with its various environments.

Assessment of the unit's organisation and life

Team 4 appears to have a complex recent history. It arises from the '*Biostatistical modelling and pharmacometrics*' strand of a research group created in 2005 as a single team on '*Models and methods for therapeutic evaluation of chronic diseases*', supplemented in 2010 by a clinical professor in infectious diseases and in 2012 by a statistician and mathematical modeller in infectious diseases. The new team, called '*Biostatistical modelling, pharmacometrics and clinical investigation in infectious diseases*' results from this evolutionary process, with a new focus on infectious diseases. Being a small team, there are no evident management issues to comment on, other than a clear problem of overload for theTeam leader, which needs to be addressed. This is due in part to the small number of senior staff with statistical expertise, which does not appropriately reflect the team's substantial research contribution in that area. Discussions with researchers and PhD students during the site visit revealed that the statisticians within the team provide highly effective and easily accessible biostatistical support for research throughout the Unit.

Assessment of the unit's involvement in training through research

The team provides good support for its PhD students, who appear well integrated into the group's mainstream research. PhD students are clearly encouraged to publish their work, and to present it at international conferences. The 4 PhD students who have completed their PhDs have all started careers in academia or industry. One specific problem identified by the team is that the tema meader carries a too heavy load of PhD supervision; this concern is warranted and clearly needs to be addressed. The current number of PhD students (10) appears healthy, and will help to foster a good research ethos within the team. The number of postdoctorants is low, though this issue is not specific to the team. Increasing the number of postdocs, and the length of time they spend in the unit to a more realistic 2-3 years so that they can develop a good publication record, is an objective worth pursuing through grant funding and collaborations.

Assessment of the five-year plan and strategy

The five-year plan represents an ambitious but coherent development of previous work. Existing strengths in methodological research in pharmacometrics, notably optimal design, model evaluation, and testing, will be supplemented by new departures in pharmacogenetics, model-based analysis of clinical trials, modelling of viral dynamics, joint modelling and adaptive trials. On the clinical side, individual responses to anti-infectives will be explored in clinical trials and cohorts in hepatitis C, HIV and influenza. Expertise will be diversified to a greater range of infectious diseases, including hepatitis D and bacteria resistant to antibiotics. The overall focus will thus shift to a more systematic attention to infectious diseases, while retaining a primarily clinical, individual focus. At the same time, the expertise currently being developed in mathematical modelling of viral dynamics will be highly relevant to other activities planned within the IAME unit, notably ecological modelling and modelling of infectious disease transmission. Indeed the project description for Team 4 mentions focusing on the emergence of new infectious diseases, control and prevention strategies, and their psycho-social impact. These aspects may require a population-based emphasis, and provide a logical avenue for further development of their research.

Conclusion

- Strengths and opportunities:

The team benefits from some great strengths, notably an excellent international reputation for original methodological and clinical research, as demonstrated by an outstanding publication record and a visible presence on the international scene. A further positive characteristic of the team is its dual focus on methodological and clinical research, which has helped ground the methodology in clinical practice. A highly commendable feature of the team's output is its investment in accessible software. The new project provides the opportunity to consolidate this reputation and extend it in new directions in infectious diseases.

- Weaknesses and threats:

The team leader is clearly overloaded, and the number of senior staff with statistical expertise is very limited for a unit of IAME's size: these two facts are undoubtedly related. The appointment of a full-time statistician/modeller will hopefully help to lighten this burden, but may be taken up in the extra work planned over the next 5 years. There is therefore a threat that the stresses in the team workload will not be alleviated. The number of postdoctoral researchers is low, as in other teams, and requires action at Unit level.

- Recommendations:

A strategy of medium-term growth is needed to expand the number of statisticians in the team, which currently does not reflect the team's substantial research contributions in that area. Perhaps this could be achieved by developing collaborations between teams, notably in the areas of dynamical and statistical modelling. Such growth would go some way to reduce pressure on the team leader, and would also reflect the team's expanding research agenda. A strategy is also needed to attract more postdoctoral fellows, perhaps with grant funding from industry, with which the team has excellent and productive links. Such a strategy might be also enhanced by communication and popularisation initiatives towards academic colleagues and also pharmaceutical companies, provided there were no major conflicts of interests.

Team 5 : Decision sciences in infectious disease prevention, control and care

Name of team leader: Mr Yazdan YAZDANPANAH

Workforce

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014	2014-2018 Number of project producers
N1: Permanent professors and similar positions	1 (0.5)	3 (1.20)	1 (0.5)
N2: Permanent EPST or EPIC researchers and similar positions	2 (1.5)	4 (1.90)	2 (1.5)
N3: Other permanent staff (without research duties)			
N4: Other professors (PREM, ECC, etc.)			
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2 (2)	3 (2.35)	2 (2)
N6: Other contractual staff (without research duties)			
TOTAL N1 to N6	5 (4.0)	10 (5.45)	5 (4.0)

Team workforce	Number as at 30/06/2012	Number as at 01/01/2014
Doctoral students	4	
Theses defended	3*	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	2**	
Qualified research supervisors (with an HDR) or similar positions	1	4

*Since 01/2011 when the Atip/avenir unit was created

**One is ongoing; has the permission to defend HDR but has not done it yet

Detailed assessments

Assessment of scientific quality and outputs

The research topics are mostly focused on HIV infection and HCV infection. The fields covered regarding these diseases are effectiveness, cost-effectiveness, and costs of clinical care and prevention in both developed and developing countries. These projects are based on clinical epidemiology methodology and analysis of large databases. The workforce of the team is composed by scientists from clinical and public health science.

Major individual and public health topics are studied regarding HIV infection and especially cost of care, screening of HIV infection in general population and in high risk populations in France and cost-effectiveness of HIV screening strategies in Europe (Portugal). These subjects are relevant regarding disease prevalence and organisation of care for infected individuals. The results of these studies have been published in peer reviewed journals, mostly in journal dedicated to infectious diseases and HIV (Clinical Infectious Diseases, AIDS, Gut, J. Antimicrob. Chemotherapy, …). The annual rate of publication is high, meaning relevant choices on research topics and productive collaborative approaches. It would be interesting to try to link these results regarding prevalence data with incidence data and dynamic of HIV infection in populations. Collaborative studies could be easily conducted with other teams in the unit. More specifically, close collaborations with biostatisticians or biomathematicians involved in infectious diseases modelisation and spreading could be easily developped within the IAME unit.

As regards HCV, the research projects are mostly focussed on treatments and access to care. Another topic explored is the determination of best time for the treatment start during the course of HCV infection in light of the natural history of the infection in the patients and the best treatment combination. HCV projects were based on national and international collaboration (USA and european countries) including developping countries (i.e. Egypt).

HIV and HCV studies provided interesting results on optimal clinical decision-making that can be applied at bedside.

Assessment of the unit's academic reputation and appeal

The reputation is very good with regular exchanges with other teams in France (Institut Pasteur, University hospitals in Paris, ISPED [Bordeaux]), in Europe, in Africa (Senegal), and USA (Boston, New Haven). The high number of national and international collaborations is a strong indicator of the work quality. The members of the team were involved in many international conferences as organizers, chairman or invited speakers. In addition, they are active members of national and international scientific societies. Since the creation of Avenir team/ATIP in 2011, 3 PhD students joined it, showing its strong atractivity.

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

Many interactions were reported with national or international agencies. No interaction with partners like pharmaceutical companies have been reported, due to disciplinary requirement for independent economic assessments. Interaction with scientific community is excellent (see above) and with academic environment as well.

Assessment of the unit's organisation and life

The organisation of the team is well described with regular meetings between scientists and strong supports for PhD students. The team was labelled ATIP/Avenir team in 2011. This transformation meant an INSERM labelisation with a substantial grant for 3 years. 2 recognized seniors scientists (PU-PH) are now joining the team for the next term.

Assessment of the unit's involvement in training through research

Many students were trained in the team. The students were in Master or PhD program. A strong commitment is done regarding the coaching and the valorisation of junior and young researchers. The students were invited to present regularly their project in local meetings and national conferences. The new INSERM labelisation as ATIP/Avenir has an attractive effect as examplified by the recent recruitment of 3 PhD students.

Assessment of the five-year plan and strategy

The research topics remain on HIV and HCV infection. Economic impact of HCV treatment are planned to be assessed in France and in some other countries. Two major topics will be added to previous research topics. These new projects are : hospital acquired infections in ICU and multi-drug resistant enterobacteriacae infection. Hospital acquired infections (HAI) is a worldwide major public health problem in term of morbidity, mortality and cost. HAI is also an important source of emerging pathogens (bacteria, viruses and fungi).

The research projects will be conducted based on patients hospitalized in acute care but also among patients hospitalized in intensive care units. The two senior scientists joining the team have very good national and international reputation on that topic. These new research fields clearly represent an added value for the team and are promising, as they rely on an access to large european databases from various ICU. It can be anticipated that this will give rise to interesting results and major publications.

In the near future, the team also plan to get involved in studies on individuals' preferences and trade-offs between risks, which would enrish the results derived from cost-effectiveness studies.

Conclusion

- Strengths and opportunities:

The recognized experience regarding HIV and HCV studies is clearly a strength, and is fully integrated in the IAME general project.

While the need for cost-effectveness analyses on HIV and HCV remains advocated, this team has the potential to be among the reference centers for these topics in France and in Europe.

The questionning on applicability of results at bedside and for daily practice is a true real value.

They have access to large databases and good interactions with other international teams.

The choice to develop a project on hospital acquired infections is valuable both for individuals and public health.

The international collaborations are also a strength, as is their very good scientific production.

- Weaknesses and threats:

Three students recently defended their PhD and a postdoctoral student spent the last 12 months in the team and efforts must be made to renew the PhD and a postdoctoral students of the team. .

Recruitment of postdoctorants for longer stay should be prioritzed.

- Recommendations:

This team is involved on topics of major interest in terms of public health, and high levels of publications have been achieved. The projects proposed by team 5 are clearly defined and the dimension of patients' preferences regarding treatment options will be investigated.

The committee encourages studies relating to issues regarding access to care in France but also through international collaborations. This team is probabely the only one in the unit who can integrate this factor in the clinical studies.

5 • Conduct of the visit

Visit dates:	24 and 25 january 2013
Start:	Thurday 24 january 2013 at 11:15
End:	Friday 25 january 2013 at 16:30
Visit site(s):	Hospital Bichat /Paris Diderot university Campus
Institution:	
Address:	Paris 75018

Conduct or programme of visit:

Day one –24January 2013

11:15 Welcome (closed-door) Visiting committee with the AERES Scientific advisor
11:25-11:40 AERES representative: the role and procedures of AERES
11:40-12:40 Director of the Unit: Presentation of the past activities and project

Lunch 12:40-13:30

13:30 14:30 Team 1 – Quantitative evolutionary microbiology (30' Talk + 30' discussion, including 5' with the team leader)
Name of the team leader Olivier Tenaillon

14:30- 15:30 Team 2 – Ecology, evolution and therapeutic of virulence and resistance in bacteria
Name of the team leader Erick Denamur

15:30-15:50 Coffee break

15:50- 16:50 Team 3 – Antiretroviral resistance, genetic diversity and therapeutic strategies in HIV infections
Name of the team leader Diane Descamps

16:50 -17:50 Parallel meetings with personnel:
Discussions with engineers, technicians, administrative
Discussions with staff scientists
Discussions with students and post-docs

17:50-18:45 Debrief of the first 3 teams

Day two – 25 january 2013

8:30-9:30 Team 4 – Biostatistical modelling, pharmacometrics and clinical investigation in infectious diseases
Name of the team leader France Mentré

9:30- 10:30 Team 5 – Decision sciences in infectious disease prevention, control and care
Name of the team leader Yazdan Yazdanpanah

10:30-10:50 Coffee break

10:50-11:30 Discussion with the representatives of the managing bodies

11:30-12:15 Discussion with the head of the Unit

12:15-13:30 Lunch

13:30-16:30 Private meeting of the visiting committee (in presence of the AERES scientific advisor)

16:30 End of the visit

6 • Statistics by field: SVE on 10/06/2013

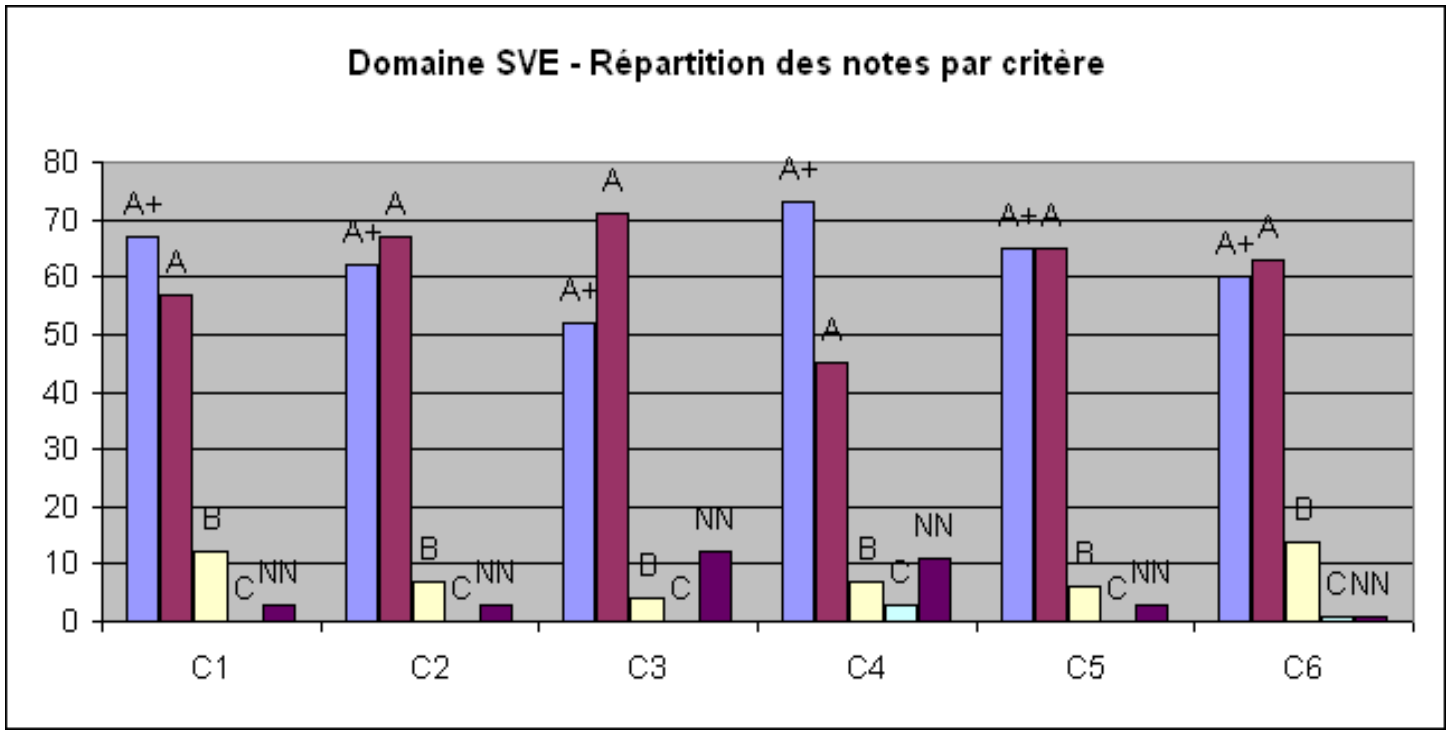
Grades

Critères	C1 Qualité scientifique et production	C2 Rayonnement et attractivité académiques	C3 Relations avec l'environnement social, économique et culturel	C4 Organisation et vie de l'entité	C5 Implication dans la formation par la recherche	C6 Stratégie et projet à cinq ans
A+	67	62	52	73	65	60
A	57	67	71	45	65	63
B	12	7	4	7	6	14
C	0	0	0	3	0	1
Non Noté	3	3	12	11	3	1

Percentages

Critères	C1 Qualité scientifique et production	C2 Rayonnement et attractivité académiques	C3 Relations avec l'environnement social, économique et culturel	C4 Organisation et vie de l'entité	C5 Implication dans la formation par la recherche	C6 Stratégie et projet à cinq ans
A+	48%	45%	37%	53%	47%	43%
A	41%	48%	51%	32%	47%	45%
B	9%	5%	3%	5%	4%	10%
C	0%	0%	0%	2%	0%	1%
Non Noté	2%	2%	9%	8%	2%	1%

Histogram



7 • Supervising bodies' general comments

Le Président

P/VB/RL/NC/YM – 2013 - 115
Paris, le 25 avril 2013

M. Pierre Glaudes
Directeur de la section des unités de l'AERES
20 rue Vivienne
75002 PARIS

S2PUR140006419 - Infection, Antimicrobien, Modélisation, Evolution - IAME - 0751723R

Monsieur le Directeur,

Je tiens en premier lieu à remercier les membres du comité de visite de l'AERES pour la production du rapport sur la situation du Laboratoire « Infection, Antimicrobials, Modelling, Evolution» (IAME), rapport élogieux qui souligne l'excellente qualité de la recherche qui y est produite, attestée par le haut niveau qualitatif et quantitatif des publications. L'originalité de son projet très intégrateur, mêlant des approches allant de la biologie moléculaire à l'aide à la décision en matière de politique de santé en passant par la modélisation, a également été soulignée.

L'université fera, à la mesure de ses moyens, les efforts nécessaires pour maintenir ce niveau d'excellence et assurer le développement des projets à venir portés par les membres de cette unité.

Je vous prie d'agréer, Monsieur le Directeur, l'expression de toute ma considération.

Vincent Berger

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