

EVALUATION REPORT OF THE UNIT

Lism - Laboratoire d'ingénierie des systèmes macromoléculaires

UNDER THE SUPERVISION OF THE
FOLLOWING ESTABLISHMENTS AND
ORGANISMS:

Aix-Marseille université - Amu, Centre national de
la recherche scientifique - CNRS

EVALUATION CAMPAIGN 2022-2023
GROUP C

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In the name of the expert committee¹:

Philippe Huber, Chairman of the committee

For the Hcéres²:

Thierry Coulhon, President

Under the decree n° 2021-1536 of 29 November 2021:

¹ The evaluation reports 'are signed by the chairperson of the expert committee'. (Article 11, paragraph 2;)

² The president of the Hcéres 'countersigns the evaluation reports established by the expert committee and signed by their chairperson.' (Article 8, paragraph 5).

This report is the result of the unit's evaluation by the expert committee, the composition of which is specified below. The appreciations it contains are the expression of the independent and collegial deliberation of this committee. The numbers in this report are the certified exact data extracted from the deposited files by the supervising body on behalf of the unit.

MEMBERS OF THE EXPERT COMMITTEE

Chairperson:

Mr Philippe Huber, Commissariat à l'énergie atomique et aux énergies alternatives - CEA

Experts :

Ms Karine Bernardeau, Inserm, Nantes (representative of supporting personnel)

Ms Isabelle Delton, Institut national des sciences appliquées – Insa, Lyon (representative of CNU)

Mr Philippe Huber, CEA, Grenoble

Mr Jean-Michel Jault, CNRS, Lyon

Mr Martin Picard, CNRS, Paris (representative of CONRS)

HCÉRES REPRESENTATIVE

Ms Ina Attrée

CHARACTERISATION OF THE UNIT

- Name: Laboratoire d'ingénierie des systèmes macromoléculaires
- Acronym: Lism
- Label and number: UMR 7255
- Number of teams: 8
- Composition of the executive team: Mr James Sturgis

SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement

SVE3 Molécules du vivant, biologie intégrative (des gènes et génomes aux systèmes), biologie cellulaire et du développement pour la science animale

THEMES OF THE UNIT

The unit works on 1/the structural and functional characterisation of multi-protein nanomachines located at the bacterial envelope (teams 2, 3, 4, 6 and 8), 2/the targets of effectors of bacterial secretion systems (Teams 1 and 8), 3/the pathogenic role of bacterial biofilms (team 5), 4/the pathophysiological roles of lipolytic enzymes produced by mycobacteria (team 7).

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The unit was created in 1992, in three CNRS buildings located at 31 Chemin Joseph Aiguier, Marseille. These buildings are shared by three other units studying molecular microbiology and several platforms constituting a research federation, the Institut de Microbiologie de la Méditerranée (IMM). The site also contains two other CNRS labs, unrelated to biological sciences and the regional delegation of the CNRS.

The unit is directed by Pr James Sturgis (also head of Team 2), since Alain Filloux has left in 2008, and the deputy director is Eric Cascales (also head of Team 8).

RESEARCH ENVIRONMENT OF THE UNIT

The four IMM units share a common thematic centred on the biology of bacteria at different scales, from the molecular machines to bacterial consortia, as well as the characterisation of giant viruses. The IMM includes several platforms, such as bioinformatics, proteomics, transcriptomics, microscopy, protein production, fermentation, NMR and EPR, making it a very attractive place to study microbiology. Lism members are involved in the management and organisation of the IMM. In particular, three Lism members are heads of the NMR, Microscopy and Transcriptomic platforms. The IMM also organises a series of invited seminars.

Within Aix-Marseille University (Amu), the IMM is part of the Institut de 'Microbiologie, Bioénergie et Biotechnologies (IM2B)', and is composed of eleven research units and several platforms. The IM2B distributes grants for selected research programs, and is involved in various educational programs, including five Masters.

UNIT WORKFORCE: in physical persons at 31/12/2021

Permanent personnel in active employment	
Professors and associate professors	3
Lecturer and associate lecturer	7
Senior scientist (Directeur de recherche, DR) and associate	2
Scientist (Chargé de recherche, CR) and associate	7
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	13
Subtotal permanent personnel in active employment	32
Non-permanent teacher-researchers, researchers and associates	1
Non-permanent research supporting personnel (PAR)	6
Post-docs	2
PhD Students	18
Subtotal non-permanent personnel	27
Total	59

DISTRIBUTION OF THE UNIT'S PERMANENTS BY EMPLOYER: NON-TUTORSHIP EMPLOYERS ARE GROUPED UNDER THE HEADING 'OTHERS'.

Employer	EC	C	PAR
CNRS	0	8	13
Aix-Marseille Université	10	0	0
Inserm	0	1	0
Total	10	9	13

UNIT BUDGET

Recurrent budget excluding wage bill allocated by parent institutions (total over 6 years)	1175.0
Own resources obtained from regional calls for projects (total over 6 years of sums obtained from AAP idex, i-site, CPER, territorial authorities, etc.)	1094.0
Own resources obtained from national calls for projects (total over 6 years of sums obtained on AAP ONR, PIA, ANR, FRM, INCa, etc.)	4189.0
Own resources obtained from international call for projects (total over 6 years of sums obtained)	18.0
Own resources issued from the valorisation, transfer and industrial collaboration (total over 6 years of sums obtained through contracts, patents, service activities, services, etc.).	0.0
Total in euros (k €)	6476.0

GLOBAL ASSESSMENT

The Lism research unit is composed of eight teams with a general common thematic on molecular microbiology. Most teams work on nanomachines located at the bacterial envelope, others on bacterial lipids, effectors of bacterial secretion system and biofilms. Research axes are consistent and focus on the structure-function of protein complexes and host-pathogen interactions.

The scientific production of the unit is very good to outstanding, depending on the team, with 117 articles published, including 79 as a leader author. The production comprises some outstanding publications (Nature, PNAS, Embo J, PLoS Biol, Nat Microb, Nat Comm, Nucl Acids Res...), notably those related to the structure and functioning of the type 6 secretion system (Teams 4 and 8) and the energy transfer of the Ton complex (Team 3). Research lines with an excellent scientific output (published in PNAS, Nat Microb, PLoS Genetics, PLoS Path, J Exp Med, Embo J., J Mol Biol, Nucl Acids Res, Mol Microb,) include the investigation of the regulation of the biofilm formation in pathogenic settings (Team 5) and of the role of lipids in mycobacterial infections (Team 7). Very good articles (published in PLoS Path, Sci Rep, mBio, J Mol Biol, Nat Comm, Oncotarget, Sci Adv, ...) have been published on the repertoire of Tat effectors and on the human targeting of a T6SS effector (Team 1), on the interaction of aquaporin with lipids (Team 2) and on various protein structures solved by NMR (Team 6).

The unit reputation is very strong at the national and international levels, as attested by numerous invitations to international meetings (70) and prizes (3 from the Fondation Bettencourt-Schueller and 1 from the SFBBM), as well as several organisations of meetings (3 international, 2 national and 3 local symposia). However, some teams should make more efforts to insert into European networks. The unit members were very successful to obtain grants from national agencies (12 projects financed by ANR as coordinator), 21 grants from charity associations and 8 from a local Labex (Amidex).

Based on unit's expertise and results, collaborations with industrial partners (Nosopharm, Sanofi, Helicityl, Adisseo) have been initiated and two patents were filed. Concretisation of these partnerships by research contracts and patent licensing is underway or should be developed. However, no collaborations were established with microbiology units in hospitals, which could benefit to unit translational activities.

The unit interacts strongly with the non-academic world, through vulgarisation articles, radio broadcasts and exhibitions in museums, as well as events like 'Fête de la Science' and in meetings with charity associations.

There is a good balance between researchers and teaching-researchers. All technical support (PAR) is CNRS staff, none are from Amu. The size of the teams is highly heterogeneous: some with only one or two researchers/teaching researchers (Teams 1,4,5,6) and two teams having no PAR (Team 3, and Team 1 in the near future), which may impede their future development. The number of PhD students (23 defended thesis, 16 ongoing) is in agreement with the supervising capacities of the unit and their publication level is excellent. This also holds true for the postdocs, but their number is low (7). The unit (teaching-researchers and some researchers, PhD students and Aters) participates strongly to the educational programs at Amu, and by providing online courses.

The unit organisation is excellent with all mandatory requirements in place, except for the meetings of the unit council that were not rescheduled since the pandemic. The common budget, coming from the recurrent institutional grants and overheads, is sufficient to maintain a good level of maintenance and renewal of laboratory equipment, which is appreciated by all unit members. This budget also serves to compensate for temporary technician loss and for Master 2 grants. In addition, the unit benefits from the environment of the IMM, located on the same campus, and which comprises three other units and numerous platforms that are useful for Lism research axes. Several parts of the buildings hosting the Lism teams have been renewed and more space has been attributed to the unit, which provided enough space for the unit to develop its activities; however, parts of the lab are still in a very bad condition, which is a real concern regarding the allocation of space, the standing towards the guests and may even constitute a security issue.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Focus on specific areas:

Except for some research axes, the unit thematic is remarkably focused on bacterial multi-protein complexes and the role of bacterial virulence factors in pathogenicity.

Applications for EU funding:

Very few applications were deposited, if any, while some topics (notably from Team 8) have a strong international positioning that could obtain European grants. This situation is assumed by the PIs of the corresponding projects, that declare that the level of funding from national agencies and charities matches their funding needs.

Attractive website:

The unit renewed its website, which is now very clear and informative although some publications were missing.

Postdocs:

The number of postdocs is still limited: seven recruited over the period (2 with short contracts), including two ongoing. Only one international postdoc (USA), for six months.

Interaction with industry:

The unit is mostly involved in basic research. However, some collaborations have been established with industrial partners: Team 4 collaborated with Nosopharm on anti-T6SS drugs; Team 5 developed collaborative research with Sanofi and Helicityl on anti-biofilm molecules; Team 6 collaborated with Adisseo for the antibacterial effects of RumC peptides; Team 1 hosted a PhD student from Novartis. Only one patent was deposited.

Non-university staff not involved in public interaction:

The non-teaching staff has been involved in numerous vulgarisation actions.

Deputy director:

Eric Cascales was appointed as Deputy Director.

Internal seminars in English:

Major improvements both at the level of IMM and IM2B.

Repetition of the retreat experience and technical/administrative stall meeting:

Not set up, because of the pandemic.

Mentoring and administrative help for grant applications:

Senior scientists and administrative staff provide comments and help for grant application to junior scientists.

Increase the number of HDR:

A large number (6) HDR have been defended during the period.

A new technical staff for the common facilities:

The replacement of the retired PAR was possible for two years by paying a CDD on Lism common funds, but no stable positions was obtained from the supervising bodies -although considered as a priority for the unit-, thus compromising the existence of the common facilities. Dish washing and media preparation is now collectively performed by Team PARs.

Focusing on projects with international leadership:

This part will be treated in the team evaluation sections.

B – EVALUATION AREAS

EVALUATION AREA 1: PROFILE, RESOURCES AND ORGANISATION OF THE UNIT

Assessment on the unit's resources

The unit was very efficient in obtaining grants from ANR, charity foundations and the Labex Amidex. Altogether, the teams and the common services obtained enough money to develop their scientific projects. Regarding human resources, recruitment largely compensated departures – except for three PARs not replaced, and two new teams were created by mobility from another lab or emergence from a Lism team. The common platforms in the unit and the institute (IMM) are excellent and in line with the research thematic. The number of PhD students is proportionate to the number of HDR, but the number of postdocs remains limited.

Assessment on the scientific objectives of the unit

The general thematic of the unit is very clear and focused, which makes the unit highly visible both at the local and national levels, with some teams having an international reputation. The unit is composed of teams of very different sizes. The Lism is very well integrated in its local environment as it belongs to the IMM institute, with whom it shares buildings, platforms and some research themes. It is thus an outstanding place to study molecular microbiology. However, the interest for the unit and its environment may be more limited for research axes in cellular microbiology, which is the case of two teams.

Assessment on the functioning of the unit

The unit follows the required institutional rules aiming at providing the well-being and security of its staff, however, the unit bylaw needs to be better diffused in the unit. The computer system is secured at the IMM level.

1/ The unit has resources that are suited to its activity profile and research environment.

Strengths and possibilities linked to the context

In terms of financial resources, the Lism benefits from its integration into the IM2B, notably by obtaining numerous grants from the Labex Amidex (5 grants for a total of 1 M€) and by the recruitment of Master students involved in the Amidex educational program. Researchers from the unit obtained twelve grants as coordinators from the ANR, for a total of 2.5 M€ which is highly significant. The unit was also very successful to obtain grants from charity associations (VLM, FRM...) for a total of 1.5 M€. Altogether, five million Euros (830 k€/y in average) were obtained from external resources, which is excellent for a unit of this size.

The recurrent funding (196 k€/y in average) from the institutions and fifteen percent of the external grants were used to purchase common equipment for the unit (purification robots, ultracentrifuges, microscopes...), to set up new platforms (P2 lab, lipidomics 'platform'), for equipment maintenance, for the salary of a technician for common services (media preparation) and to pay the gratification of M2 students (10). As most teams are focused on molecular microbiology, the platforms can be used by several teams. Overall, this is an excellent and efficient use of unit common money.

The permanent human resources are well balanced with nine researchers from CNRS/Inserm, ten teaching-researchers from Aix-Marseille University; thirteen tenured PARs were present at the end of 2021, all from CNRS, and six additional non-permanent PARs (and numerous technicians/engineers in CDD in previous years), indicating that external grants are partly used to hire technicians to support dedicated programs.

In conclusion, the unit has enough financial and human resources (however more limited for PARs) to accomplish its research programs.

Weaknesses and risks linked to the context

Despite numerous external grants, only a few postdocs were hired, although they could boost the scientific production and bring new concepts and techniques. This situation is notably due to the lack of PAR in some teams for which grants are used to hire engineers instead of Post-docs. This is clearly a problematic situation as it is detrimental to the maintenance of a long-term know-how and practical expertise.

Three CNRS PARs left or will leave soon the unit for retirement or mobility and there is no guaranteed replacement plan (the joining PARs came with the new team: Team 7), leaving two teams without PAR.

There are no Amu PARs in the unit, while the teaching activity is very high: ten ECs and in general several teaching PhD students (monitorat) as well as ATERS.

2/ The unit has set itself scientific objectives, including the forward-looking aspect of its policy.

Strengths and possibilities linked to the context

As indicated by the unit director, the main objective of the unit has been to study the multi-protein complexes of the bacterial envelope since 1992, with the characterisation of recently discovered nanomachines and the implementation of cutting-edge techniques. The unit is very well integrated in its scientific environment, with fruitful interactions with other units of the IMM and strong use of several IMM platforms. The environment of the unit is excellent because of the numerous local research entities centred on microbiology, and more specifically in the structural microbiology field. The general scientific thematic of the unit is well centred and most research programs are coherent with this thematic.

Team organisation seems flexible, with the emergence of a new group (Team 4) from Team 8; the integration of the remaining group of a PI who left the unit in 2018 into Team 8; the arrival of two large teams in 2018 (Team 7) and in 2022 (not evaluated in this document). Decisions regarding the evolution of the unit is made collegially by the director together with the group leaders.

Weaknesses and risks linked to the context

The unit is composed of teams of very different sizes and varying levels of scientific reputation, which can influence decisions at the unit level and, even more so, overshadow the smaller teams.

The research axes that are not directly related to the study of macromolecular complexes may not benefit as much as others from the platforms and the scientific context.

3/ The functioning of the unit complies with the regulations on human resources management, safety, the environment and the protection of scientific assets.

Strengths and possibilities linked to the context

The Lism unit has a rather good parity level. For all members excluding students: 60/40 (in female/male ratio); for PhD students: 41/59; for group leaders: 33/67. The unit complies with non-discriminatory rules for recruitment, as issued by the CNRS. Working conditions are evaluated every year for each worker, and a health and safety assessment document is filed by the unit safety officer. The technical staff has individual meetings every year with his group leader to assess carrier management, training possibilities, safety issues, and to evaluate and prevent psychosocial risks. Recommendations for promotions are established by a small committee of four members (including 2 PARs), following the meetings with the technical staff.

The unit computer system is secured at the IMM level. The unit has implemented new procedures to improve the environmental impact of the functioning of the lab.

There is no formal Business Continuity Plan established by the unit, however critical areas and priorities have been delineated during the Sars-Cov2 pandemic to cope with emergency situations.

The unit benefited from extensions and renewal of some lab spaces.

The staff of the unit are very happy with their working conditions and emphasise the ease of sharing knowledge and technical skills.

Weaknesses and risks linked to the context

No unit council took place since the end of the pandemic.

The informal rules and bylaw that have been elaborated in the unit will need to be updated because of the increasing size of the unit and to comply with new management rules. Moreover, the distribution of these rules seems to be erratic.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The unit has an excellent national visibility, attested by numerous grants from ANR and charities. However none was obtained at the EU level, while some teams have a clear international leadership. The other teams should be more active at establishing European networks. The unit is attractive because of its knowledge and several top-range platforms. Unit members participated in several national scientific and steering committees, organised meetings and strongly participated in teaching. The number of PhD students is proportionate to the unit size, but the number of postdoc was very limited. Some PARs were not replaced, leaving teams without PAR.

1/ The unit has an attractive scientific reputation and contributes to the construction of the European research area.

Strengths and possibilities linked to the context

The Lism unit has a high national reputation that has been built over the years. Some teams are also international leaders in their field. The unit organised three international meetings, as well as two national and three local symposia, which is a good way to gain in visibility. The head of the unit stayed in Nigerian and American Universities. Members of the unit participated in six consultations for national or regional agencies. The teaching activity of the teaching-researchers and some researchers is impressive. A large number of lessons for students of different levels has been recorded by these members and can be downloaded. Unit members (PIs and students) have received six prizes from learning societies or foundations.

All group leaders were invited to national meetings, and most, to international meetings.

The unit members participated to fourteen editorial boards of middle to high-range scientific journals or collection series, which is high for the unit size; The PI of Team 8 contributed to eleven of them. Members also participated to steering and scientific committees at the national and European levels, notably at the CNRS and CNU.

The unit formed 39 PhD students (21 who defended and 18 ongoing), which is proportionate to the number of C/EC in the unit. The Lism implemented a granting system to hire selected M2 students.

Weaknesses and risks linked to the context

No European grant was obtained by the unit during the period, and little effort has been made in that direction. The number of postdocs is minimal, and almost exclusively French. Similarly, PhD students were mostly local candidates.

Except for Team 8, all other group leaders should gain in visibility internationally and be more present at the European level.

2/ The unit is attractive for the quality of its staff hosting policy.

Strengths and possibilities linked to the context

During the period, two permanent researchers and one EC were recruited, three permanent researchers/EC were integrated by mobility from other labs. Five PARs from CNRS were recruited or joined the unit by mobility. Among these new members, five formed a new team (Team 7). In addition, a new team joined the unit in 2022 (see unit website). Conversely, four researchers left the unit for retirement (2) or mobility (2) and three PARs. The recruitment balance is thus very positive for the unit, and is a very good indicator of the unit attractiveness, in addition to its capacity to recruit young researchers and PARs at CNRS mostly and Inserm (1). The Lism keeps applying every year for tenured positions at the CNRS and university.

Nine PARs were promoted during the period and promotions concerned all PARs except for the newcomers and those at the end of carriers. PAR promotion is thus actively supported and well balanced.

Weaknesses and risks linked to the context

The unit had less success to recruit staff from the University (1 EC in 2019). Most strikingly, there is no permanent PAR from the University, while 10 EC are present in the Lism, as well as numerous PhD students with teaching duties and some Aters.

The technician for common services (media preparation...) was not replaced.

3/ The unit is attractive because of the recognition gained through its success in competitive calls for projects.

Strengths and possibilities linked to the context

The unit had a lot of success for the highly competitive ANR grants: twelve were obtained by different members of the unit and all as coordinator. Similarly, 21 grants were obtained from charity associations (VLM, FRM...) and eight from the Labex Amidex, both by several unit members.

Weaknesses and risks linked to the context

No European funding was obtained, and some Lism members did not show a good capacity to join European/international networks.

4/ The unit is attractive for the quality of its major equipment and technological skills.

Strengths and possibilities linked to the context

The unit is attractive in terms of equipment and technologies thanks to all the platforms, available within the Lism but also at the IMM, and because of strong skills to study molecular microbiology. The platforms include: fermentation, protein production, NMR, spectroscopy, genomics and proteomics, electron and fluorescence microscopy, EPR spectroscopy, lipidomics in addition to recent unit equipment (microscopes...). These platforms are ruled by qualified technicians and the equipment is maintained thanks to the common budget. The equipment level is thus excellent in the unit and its environment.

Weaknesses and risks linked to the context

No real weakness in this domain. A solution for the replacement of the NMR console must be found to keep this equipment paramount for the unit and the NMR platform.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The unit has a high level of publication in middle to top-range journals; however, there is a large heterogeneity between teams. All researchers and teaching-researchers were publishers. PhD students and postdocs also have a high level of publication, most often as the first author. The scientific studies comply with the rules of scientific integrity; datasets in genomics, transcriptomics and 3D structures are deposited in accessible public databases. Proportion of open-access articles is very good and most, but not all, manuscripts are deposited in open-access platforms.

1/ The scientific production of the team meets quality criteria.

Strengths and possibilities linked to the context

All original articles were published in peer-reviewed journals. Articles were published in middle-range (BBA, Frontiers, J Bact, Plos One...) to high-range (PLoS Path, mBio, ...) to top-range (Science, Nature, PNAS, Embo J, Sci Adv, Nat Microb, Nat Comm, Nucl Acids Res...) journals. Overall the publication level is excellent.

Weaknesses and risks linked to the context

No weakness in this area.

2/ Scientific production is proportionate to the research potential of the unit and shared out between its personnel.

Strengths and possibilities linked to the context

The unit published 119 articles during the period. Unit members were in leader positions in 79 articles, which yields an average of 6.3 articles per researcher. In addition, 36 reviews/editorials/letters were published, for some of them in top-range journals (Cell, Molecular Cell, Nat Microbiol...). All researchers published and all ECs are authors of publications (sometimes in leader position), even those recently recruited. PhD students were co-authors of 66 articles, which corresponds to an average of 3.1 articles per PhD students with a defended thesis with frequent first authorship. This is a remarkable publication level for the students. Similarly, each postdoc published several articles, which is remarkable given the short time they have in the lab.

Weaknesses and risks linked to the context

Publication level is highly variable between teams, with teams publishing top-range articles, and teams publishing in more specialised journals.

3/ The scientific production of the unit complies with the principles of research integrity, ethics and open science.

Strengths and possibilities linked to the context

The unit does not perform research involving humans, nor animals or very indirectly. Therefore, the unit is not exposed to ethical issues.

The PhD students are trained for integrity in science at the doctoral school level and all are required to take this course. The unit direction and teams seem to be aware of integrity issues, especially in image manipulation.

Genomic, transcriptomic and structural data are deposited in appropriate public databases.

Weaknesses and risks linked to the context

Although most data are noted in numbered notebooks, spectroscopy and microscopy datasets are not traced and organised in specific storage.

Twenty-eight publications out of 155 (articles + reviews) are not accessible in open access, which is quite high, and deposition in Hal repository is team-dependent.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

Assessment on the inclusion of the unit's research in society

Although the unit is focused on basic science, several collaborations have been established with industries to develop anti-virulence strategies, taking advantage of team results and know-how. However, only a few contracts were established with industrial partners. Also, interaction with hospital microbiology units could lead to a better breakthrough in translational research. Interaction with the general public is excellent, notably with pupils, in various regional and national manifestations, radio broadcasts, social networks and prestigious exhibitions.

1/ The unit stands out by the quality of its non-academic interactions.

Strengths and possibilities linked to the context

Team 4 established a partnership with Nosopharm to identify anti-T6SS drugs in the context of antibioresistance that seems to be well-engaged. Because of the important role of the T6SS in the gut microbiota homeostasis, this collaborative project may result in important medical benefits. Team 5 developed fruitful interactions with Sanofi and Helicityl for testing drugs inhibiting biofilm formation through their ability to image biofilm by confocal microscopy. This is a very important project, notably for *P. aeruginosa* infections of cystic fibrosis patients. Team 6 interacts with Adisseo for the development of antimicrobial peptides with complex structures in the context of animal gut infections. In this partnership, developed through an ANR grant, the team determined the peptide structure by NMR. A patent was recently filed (12/2021) by Team 7 on the use of another set of antimicrobial peptides. More time is required to see whether the patent is licensed and if it leads to industrial interactions. Team 7 also participated to a patent on the use of mycobacteria labelling compounds.

Weaknesses and risks linked to the context

Although the microbiology field may lead to strong interactions with industries, some scientific projects remain mostly in the field of basic research and the efforts made to valorise research products could be increased.

2/ The unit develops products for the socio-economic world.

Strengths and possibilities linked to the context

The unit interacts strongly with charity associations (VLM, Espoir contre la Mucoviscidose, FRM) and foundation Bettencourt, as attested by the numerous grants obtained, and participates to meetings organised by VLM and Espoir contre la Mucoviscidose.

Weaknesses and risks linked to the context

There is no interaction with microbiology units in hospitals, which could increase the unit interest for translational research.

3/ The unit shares its knowledge with the general public and takes part in debates in society.

Strengths and possibilities linked to the context

The unit shares its knowledge in numerous public events, such as the Fête de la Science, the Nuits des Chercheurs, ... and communicates to young pupils in several collèges and lycées, or hosts for days or weeks pupils in third grade, for the discovery of scientific professions. The T6SS work led to Team 8 participation in major exhibitions (9 months at the Museum d'Histoire Naturelle de Dijon; 8 months at the Palais de la Découverte, Paris), in vulgarisation articles in Sciences et Vie Junior and in a radio broadcast 'L'Edito au carré' at France Inter. The head of the unit and a team leader participated to a local TV interview in the framework of the Igem project. The unit also published articles and videos (CNRS YouTube channel) on the therapeutic strategies against Sars-Cov2. The unit also communicates through social media such as Twitter.

Weaknesses and risks linked to the context

No weakness in this area.

C – RECOMMENDATIONS TO THE UNIT

Recommendations regarding the Evaluation Area 1: Profile, Resources and Organisation of the Unit

A solution should be found for the two teams having no technical help, notably by applying to Amu tenured positions.

Collaborations with microbiology units in hospitals should be established.

More postdocs could be hired.

Make sure that the unit bylaw is updated and distributed to all unit members, especially to the newcomers.

Reschedule council unit meetings.

Recommendations regarding the Evaluation Area 2: Attractiveness

European networking should be reinforced.

Some team members could apply to European grants.

Recommendations regarding Evaluation Area 3: Scientific Production

Some teams should increase their publication levels.

Article deposition in Hal should be systematic.

Recommendations regarding Evaluation Area 4: Contribution of Research Activities to Society

Consolidate collaborations with industries.

TEAM-BY-TEAM ASSESSMENT

Team 1: *Pseudomonas aeruginosa* Pathogenicity
 Name of the supervisor: Ms Sophie Bleves

THEMES OF THE TEAM

Team 1 focuses on *P. aeruginosa* virulence factors, through the determination of the effectors of the Tat export system and by exploring the action of exotoxins secreted by the Type 6 Secretion System.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team is relatively small and could increase their impact by focusing on fewer topics.

The team focused on two topics (Tat export system and Type 6 Secretion System) instead of three (Tat, Type 6 and Type 2 Secretion System), but it has lost one of the researchers who carried on the third topic.

Aim to increase visibility by international conference organisation and by applying for collaborative grants.

Team 1 organised international (1) and national (1) meetings. Collaborative grants were obtained from a local foundation (2), from a charity association (3) and from ANR (1), all as project leader.

The committee recommends continuing to develop industrial collaborations and the excellent links with the local charity.

Industrial collaborations were not maintained.

Continue to collaborate across the team.

Several co-publications attest to the collaboration between team members.

The committee strongly recommends that the young researcher gets her HDR.

The young researcher obtained its HDR.

The team should continue to collaborate to progress the work most effectively but ensure that they retain intellectual control of the projects.

Collaboration is very active and productive; however, team members are not or rarely in leader positions in publications resulting from these collaborations.

The team should explore funding opportunities to increase its size. Pseudomonas aeruginosa is one of the six major Eskape pathogens that show worrying levels of antibiotic resistance. Since antimicrobial resistance is a priority area for European funding, the group should be encouraged and supported to seek funding for their work under this umbrella.

Team 1 thematic on *P. aeruginosa* virulence factors was effective to obtain grants from a charity association, a Labex (A*MIDEX) and ANR, but not from the EU.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	1
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	3
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	0
Post-docs	0
PhD Students	3
Subtotal non-permanent personnel	3
Total	6

EVALUATION

Overall assessment of the team

Team 1 is a dynamic team with a well-focused and original thematic. The team leader is recognised in the field of *P. aeruginosa* biology and pathogenicity. Production is very good for a team of this size, but must be increased to obtain an international stature and to be more attractive. Team funding is variable, but increased in the last years. When the toxicity of the studied virulence factors will be better established and understood, industrial collaborations must be sought to examine the potential medical benefits of this work.

Strengths and possibilities linked to the context

Team 1 developed two related projects carried by the two researchers of the group, and focused on *P. aeruginosa* virulence. The repertoire of effectors of the Tat export system has been investigated by elegant methods and has a real interest in the field. Similarly, the finding that a T6SS effector can target and affect eukaryotic cells is new for *P. aeruginosa*. Altogether, the work of the team is important for the field and should be pursued.

This is a dynamic team, establishing national and international collaborations and organising national (1) and international (1) meetings. The PI is invited in international (3) and national (6) meetings. This is a very good acknowledgment for a small team.

An ANR grant was recently obtained as coordinator for the T6SS effector project, which will amplify the project and should eventually lead to medical benefits.

Team 1 published twelve publications (including 6 with leader positions and excluding the publications of the researcher who left the team in 2017). This is a rather good publication rate for two researchers. The PI also published editorial articles and 2 reviews, demonstrating further her recognition in the field.

The ratio of PhD students (5)/researcher (2) is normal for the six-year period, and should even increase with the recent HDR graduation of the young researcher. Two PhD students have defended their thesis with at least one article as first author for each, and three as co-author for one of them. The PAR of the team is co-author of some publications. Altogether, the management of the PhD students and the PAR seems to be adequate.

The two researchers (mostly the PI who is University professor) contributed to a high number of teaching at the Amu, and participated to evaluation committees at various levels, including for PhD and HDR. This is an excellent contribution to student education for a team of this size, and a good opportunity to select high-level students.

The two researchers participated in debates with patients of charity associations.

Weaknesses and risks linked to the context

Team 1 publishes in middle to high-range journals: Plos Pathogen, Frontiers journals, Cell Microbiology, J Mol Biol, Scientific Reports... However, team members were not in leader positions for publications in more recognised journals (except for the Plos Path in co-corresponding author). Some articles of the team that were published in high to top-range journals were produced by the researcher who left the team in 2017.

Team 1 thematic on T6SS effectors, is relatively isolated in the unit that poorly works on human hosts.

The departure of the unique PAR in the near future will affect the functioning of the team.

RECOMMENDATIONS TO THE TEAM

The main recommendation of the committee is to increase the level of publication.

Team 1 should also dedicate more effort to obtain additional national (or even European) grants to secure their functioning.

Team 1 should connect with local teams in the field of cellular microbiology and host-pathogen interactions.

Team 2: Dynamics and Assembly of membrane proteins
 Name of the supervisor: Mr James Sturgis

THEMES OF THE TEAM

The projects of team 2 are focused on understanding the role of membrane environments to regulate the structure, dynamics and functions of proteins. Three major models are investigated using both computer simulation and experimental approaches of biochemistry/biophysics: the aquaporin Z AqpZ, the Bacterial photosynthetic apparatus and mitochondrial anion channel, VDAC.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

-do not disperse in too many collaborative projects

The team has dropped several collaborative projects, but works on three independent research subjects for three researchers may be still difficult to carry out.

-the team should continue and extend its efforts on the international arena, this should include a program for the invitation of international guest students, postdocs, and visiting professors and to obtain new grants,

The team has maintained international collaborations and hosted an international student; another one postponed due to Covid should integrate the team soon;

-the committee recommends improving local interactions

Several projects involving local interactions have been funded and produced results

-it would be important to set up more regular lab meetings,

The team now has weekly meetings; interne interactions should be maintained, especially to facilitate the integration of the recruited CR.

-the team has very good potential to welcome international postdoctoral fellows,

The team welcomed a postdoctoral fellow who has now been recruited in the team,

the MCU should apply for the HDR soon,

The recommendation still applies.

-the small size of the team is clearly its main weakness and the direction of the unit by the team leader requires work and energy that is not spent for the team,

A new researcher has been recruited;

-the presence of a deputy director is essential to support this excellent team,

A deputy director was appointed.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	1
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	4
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	0
Post-docs	0
PhD Students	3
Subtotal non-permanent personnel	3
Total	7

EVALUATION

Overall assessment of the team

This is an excellent and dynamic team with original and innovative projects that rely on modelling and experimental tools to study protein assembly and functions.

Scientific production is very good to excellent, especially for a small team of which two members have teaching duties.

The attractiveness for students and collaborations is very good. The team leader teaches internationally and oversees the Igem team.

The team is very active in communication with students and the general public.

It has obtained significant funding, which is also indicative of very good recognition and visibility.

Strengths and possibilities linked to the context

Team 2 has developed three separate projects led by the three researchers in the group. The converging point is to better understand the role of membrane environments to regulate the structure, dynamics and functions of proteins. Different proteins are taken as a study model; models historically mastered by the team, new models recently developed as well as modelling approaches. Team 2 is very well recognised for its research activities and has obtained several major grants as principal investigators (ANR, Amidex, FRM, Espoir contre la mucovicirose).

Team 2 declared a total of fourteen publications (but 22 are listed in the Hcéres table and 10 on the website - this is to be specified) in medium-high-end journals that are appreciated in its field of expertise (Biochemical and Biophysics Acta-biomembranes, Journal of bacteriology, Journal of physical chemistry, Genetics); two articles are published in the prestigious journals (Nature comm and Physical review).

This is a very good to excellent level of publication for four permanent staff, which reflects good doctoral activity (22 publications listed in the Hcéres table, 15 of which include doctoral students as co-authors). The doctoral student (3)/researcher (3) ratio is reasonable for two members with teaching responsibilities and one recently recruited member.

The team contributes to scientific dissemination mainly through the national 'science festival' event. It has relatively few implications at the socio-economic level. However, two members of the team were experts for the OMNT (Observatory of Micro and Nano Technologies) and the administrations of two French Regions. The team has expertise in norms, standards, procedures recognised by the competent bodies (Iso, Afnor, FAS, etc.).

The team is very attractive to students (the team has hosted many internships). It is involved in the Igem competition which has very good international visibility (supervised by the team leader). The high attractiveness of the team is also reflected in numerous collaborations at local, national and international level.

Weaknesses and risks linked to the context

The contribution of the team for the two articles published in prestigious journals (Nature Com, PRX) is unclear - the team member(s) are placed as penultimate author, which can be considered co-PI.

The number of publications by students who have completed their thesis is heterogeneous (can vary from 1 to 8).

Team 2 has hosted many undergraduate students, which probably reflects its good attractiveness, but it may require too much supervision time for team members.

The newly hired CR is starting a new, otherwise ambitious and very competitive project. If strengthening her position (recruitment of a PhD student, ITA support, funding) is not considered a priority, integration can become fragile.

Conducting three relatively independent projects with three permanent researchers including two members with teaching responsibilities and one as unit director may be a risky challenge.

RECOMMENDATIONS TO THE TEAM

Team 2 should continue its publishing activities at the same very good to excellent level. The website should be updated for the publication list

Team 2 must provide a good environment to promote the integration of the recruited RC either by recruiting a doctoral student or a postdoc to help her develop her project, or by reorganising the team's projects. It is a question of not weakening the newly recruited CR.

The MCU will need to get its HDR.

Team 3: Molecular transport across the bacterial cell envelope

Names of the supervisors: Mr Denis Duché and Ms Laetitia Houot

THEMES OF THE TEAM

This team works on the Ton and Tol complexes from Gram negative bacteria, two huge machineries that span the inner membrane and the periplasm to reach the outer membrane. It seeks to understand how the proton motive force provided by the inner membrane is converted to mechanical work for the whole machinery. It also analyses the mechanism by which the filamentous phage is imported through the outer membrane by the Tol-Pal system.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

the team's reputation would become even stronger by an increase in the number of invited talks at international meetings for presenting the superb new structure that has been recently published.

As already point out in the report by the Director of the unit, 'this remarkable protein structure has been largely presented by the American collaborators of the team especially since the retirement of the former French PI' *involvement in the science fairs or interactions with school classes are encouraged.*

Young members of the team are involved in interactions with school classes.

the younger members of the team should think of getting their HDR as soon as possible,

One has obtained its HDR and another one is in preparation.

it is recommended the team recruit postdoctoral fellows and students in order to develop the projects,

Several students and research engineers (two on CDD) were hired during the contract. One PhD student defended her PhD (in 2018) and one is present in the team. No postdoc was hired during the evaluated period since the team focused its recruitment on engineers as the only PAR who was present in the team left the unit in 2018.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	2
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	0
Subtotal permanent personnel in active employment	4
Non-permanent teacher-researchers, researchers and associates	1
Non-permanent research supporting personnel (PAR)	0
Post-docs	0
PhD Students	1
Subtotal non-permanent personnel	2
Total	6

EVALUATION

Overall assessment of the team

This is an excellent team, with a strong background in membrane protein biochemistry which made a seminal contribution to the Ton complex structure-function relationship.

Strengths and possibilities linked to the context

This team has a strong background in genetic and protein biochemistry which is completed now by microscopy techniques. It made a seminal publication on the structure-function and the stoichiometry of the Ton complex (Nature 2016; coll S. Buchanan, NIH) with a follow-up in 2019 (Comm. Biol.).

The scientific production is excellent as fourteen original research articles were published in international peer-reviewed journals including Nature 2016; Comm Biol 2019; JMB 2019 and 2022; J. Bact. 2020; JBC 2017, where the team members play a leading role (9 as first and/or corresponding authors).

The attractiveness of the team is very-good as a MCU joined the team in 2020 with expertise in Fluorescence microscopy. To strengthen this approach, the team also collaborated with T. Mignot (LCB, Marseille) who is an expert in Time-lapse fluorescence microscopy in bacteria.

Two project financed by ANR were obtained as coordinators (the last one ended in 2021) and also an IM2B funding for 2022/2023 (30 k€). The team has three international collaborators (two in the USA and one in Germany).

The renewal of the former PI (now emeritus) by two young co-PI has been endorsed.

There are two MCU in the team, one is the co-PI, who are heavily involved in teaching duties and responsibility at Amu (450 hours/year of teaching). One of them is in charge of an international microbiology training for Ph. D students, 'Innovative teaching Plinius cursus' (since 2018) and is the International Relation referent in Biology of Amu. The team is also deeply involved in training students in entrepreneurial projects (participation in the international synthetic biology competition, Igem, since 2017). Besides the scientific training and the mentoring of the students, one of the MCU is also involved in securing funds to support such projects.

Apart from the Igem training with a clear goal towards entrepreneurial projects, the team participates in communication to a wider public audience through the Science Fair (3 years), 'Lism at school' (2 years) and welcome high-school students for one-week internships to discover science (7 students).

Weaknesses and risks linked to the context

The team could try to recruit more PhD students: only one was recruited lately (in 2021) and one defended her PhD in 2018, although team members are involved in the supervision of Master students (3 M2 and 7 M1). No technical staff is present nowadays in the lab as the only PAR left the team in 2018 (he got a position at the NIH). This could jeopardise the team future and imposes some choice about the recruitment on ANR grants (technical staff instead of PhD or Postdocs are recruited).

The last ANR ended in 2021 and the current grant is rather small for two years (30 k€). The participation of team members to international meetings appears limited in particular for talks although the Covid pandemic was not a favourable period for that.

RECOMMENDATIONS TO THE TEAM

The team should update its website for the publication list: mid-October the JMB 2022 was not included on the website, like the Comm. Biol 2019 paper, which was otherwise provided in the document to Hcéres committee. Likewise, the J.Bact paper in 2020 is not on the website of the team. This might help to increase the team visibility, including that of the two new co-PI, and potentially attract more students to do a PhD in the lab.

With the arrival of a new team in the unit which works on structure-function relationship of bacteriophage proteins, this might create an opportunity to collaborate.

Team 4: Virulence Nano-Macromolecular Machinosome
 Name of the supervisor: Mr Eric Durand

THEMES OF THE TEAM

The team works on nanomachines, in particular the Type 6 Secretion System (T6SS) of pathogenic bacteria, to understand how they are assembled and function. Knowledge of this machinery at the atomic level is then used with the goal to interfere with their normal assembly/functioning by using designed inhibitors, notably peptides.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

It does not apply since this team was recently created (2020).

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	0
Subtotal permanent personnel in active employment	1
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	1
Post-docs	0
PhD Students	2
Subtotal non-permanent personnel	3
Total	4

EVALUATION

Overall assessment of the team

Although this team recently emerged from Team 8, the scientific production of the team leader has been outstanding so far and this new team already obtained very exciting result in the field of host-pathogen interactions and the inhibition of the T6SS machinery.

Strengths and possibilities linked to the context

This is a very recent new team that started in 2020. The PI has a long-standing experience in Biochemistry and Structural Biology of proteins. He obtained outstanding results in its former lab (Team 8 of Lism) and in particular on the role of the TssA protein to initiate the tail tube polymerisation of the T6SS in *E. coli* (Nature 2016 (2nd

position and co-corresponding). He also published two papers in Nat Microbiol, one in 2017 and one in 2018 (he is last author for this one) and also an Embo J, 2019 where he is co-corresponding author (coll. Bordeaux). He is also the last author of a JMB article (2016). Since the PI started his new team, he got an ANR grant as a coordinator. This new team already obtained very exciting results on the T6SS of the Enteroaggregative E. coli pathogen. In particular, they targeted a protein/protein interface to identify a cyclic peptide inhibitor that blocks the assembly of the base plate of the T6SS nanomachine (mBio, 2021).

The PI has two very productive collaborations with a team at MMSB, Lyon and a team at IECB, Bordeaux. In addition, the team has collaborations with two Lism teams.

The team is quite attractive since it has already recruited two PhD students; the PI got an ANR grant to secure its research and was also a coordinator of a previous ANR grant in his former team. The PI has an excellent visibility both at the national and international level: he is in charge of the Electron Microscopy panel at the User Committee of Frisbi (French Infrastructure for Integrated Structural Biology, since 2018) and he was elected at the CONRS committee (section 20) in 2021. Since 2022, the PI is an associate editor at Frontiers in Cellular and Infection Microbiology.

The team is strongly engaged in translational studies in partnership with the Nosopharm company, with the goal to find alternative strategies to combat multidrug-resistant bacteria. In addition, the team collaborates with clinicians (CHU Limoges) and also with the CRCM in Marseille to screen for new inhibitors of the T6SS machinery.

Weaknesses and risks linked to the context

The team is not involved in science outreach towards the general public.

No 'significant' weaknesses were identified except that the team is rather small, but this is quite frequent for an emerging team.

RECOMMENDATIONS TO THE TEAM

The team should pursue its work at this excellent-to-outstanding level.

Team 5: Sensing environment & community lifestyle in *Pseudomonas aeruginosa*
Name of the supervisor: Mr Christophe Bordi

THEMES OF THE TEAM

This team focuses its research on bacterial biofilm formation with a special emphasis on the mechanisms that trigger this lifestyle in an opportunistic pathogen, *P. aeruginosa*. This community behaviour is a serious impediment to treat chronic infection as it reduces the efficacy of antibiotic treatments, so the team also develops innovative strategies against the formation of Biofilm.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

'continued funding support and facilitated access to PhD students may further help the development of the team'

The team has trained two PhD students who defended their thesis (2018 and 2020) and two PhD students are ongoing.

'funding is necessary to attract postdocs.'

One Postdoc was recruited (2015-2018).

'efforts should be made to increase the number of permanent researchers'

No additional permanent researchers were recruited.

'the MCU who will join the team should be strongly encouraged to apply for HDR'

The MCU got her HDR and was promoted to HC.

'attracting new researchers/postdocs will be essential to achieve this five-year plan'

This has not been achieved.

'the technician of this team (50% time) is also in charge of media and wash-up for the whole Lism unit and the committee feels that some reorganisation/recruitment to allow this technician to dedicate 100% of her time to focus on microscopy would be beneficial to this team'

a new organisation of the media's preparation has recently been established to allow the technician to dedicate more time to the team.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	1
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	0
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	3
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	0
Post-docs	0
PhD Students	1
Subtotal non-permanent personnel	1
Total	4

EVALUATION

Overall assessment of the team

This an excellent small team with only Amu staff members as researchers, that has a very good-to-excellent scientific production and very strong links with industrial partners.

Strengths and possibilities linked to the context

The team uses a combination of genomics, structural biology and fluorescent microscopy approaches to unravel the regulatory pathways, in particular the two-components systems, that trigger biofilm formation. The team develops a new technique to visualise biofilm formation by confocal microscopy that is particularly useful to screen for new inhibitors of this process.

During the evaluation period, the team published sixteen research articles/reviews. Some of them were released in high impact journals with team members in key positions including NAR 2021; Sci Rep 2019 & 2017 and PLoS Genet 2016. The team also collaborated to a work published in Nat Microbiol. 2017. Given the small size of the team and the strong involvement in the teaching of the two researchers, the scientific quality is very good-to-excellent with a strong visibility at the local and national level. One of the team members was elected at the CNU, section 65 (since 2018), is the scientific coordinator of the genomic platform (IMM, since 2012) and is in charge of the program Tiger research (2021-2029) from Amu (PIA4). This team is strongly engaged in teaching at the master and PhD level – Head of the ' Structural biology, genomic' Master program – and this represents an opportunity to attract new PhD students. The team had two international collaborations (Imperial College, UK) and University of Sao Paulo, Brazil that led to joint publications and several national collaborations including one with the CERMAV, Grenoble and the CHUR de Lille.

The team hosted four PhD students (two who defended their thesis and two are ongoing) and one postdoctoral which is fairly good given the small size of the team. Of special note are the two successive promotions of the PAR in this team, in addition to the promotion of the PI as Professor and the MCU as HC.

This team is also deeply involved in translational research through the development of anti-biofilm molecules in collaboration with two industrial partners (Sanofi and Helicityl).

Weaknesses and risks linked to the context

There is no full-time researcher in the team. Only one ANR grant was obtained previously as a partner (ended in 2018) and apart from an IM2B PhD fellowship (2021-24), there are no grants that will secure the funds of this team after 2022: one Amidex grant as coordinator ended in 2021 and one IM2B' Cluster 'grant also as coordinator will end in 2022.

RECOMMENDATIONS TO THE TEAM

The team website does not appear to be updated as two publications of the PI (as collaborative work) did not appear there.

As mentioned in the report, there is a clear perspective of patent on the molecule that inhibits biofilm formation so the team must keep this objective in mind and gets all the help it needs to reach it.

Of course, it would be beneficial for this team to recruit/attract another scientist, especially a full-time researcher and to secure ANR grants for the future.

Team 6: NMR of molecular assemblies
Name of the supervisor: Ms Latifa Elantak

THEMES OF THE TEAM

Team 6 is interested in the structural study by NMR of macromolecules involved in important biological targets such as bacteriocins (antimicrobial peptides that are promising alternatives to antibiotics) or Galectin-glycoprotein interactions at the cell surfaces.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

'Efforts should be made for securing grants and attracting postdocs.'
Several grants over the evaluation period that have allowed development of the team.

'the committee recommends more involvement in the dissemination of science and technology'
team members have been invited to international conferences – + 'fete de la science' –

'Efforts should be made to increase the number of permanent researchers'
No permanent researcher has joined the team but a research engineer has been recruited.

'Care should be taken to continue a steady recruitment of students'
Team members have significant teaching activities at the master level.

"Avoid dispersion, focus should be made on the development of the biochemistry/cell biology, oriented towards NMR requirements"
The PI has focused on a small number of projects over the last years.

"the committee fully supports the continuation in the long term of a NMR team in this environment; therefore, the maintenance of a good quality NMR spectrometer (presently 600MHz with a cryoprobe) is of paramount importance"
Renewal of the spectrometer console has been a priority of the unit and the institute for the last years – but unfortunately they have not been able to raise the necessary funds.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	0
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	2
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	1
Post-docs	0
PhD Students	1
Subtotal non-permanent personnel	2
Total	4

EVALUATION

Overall assessment of the team

This is a very good team with an excellent visibility. The scientific production is very good (18 publications), in journals covering the fields of biochemistry (PNAS, Sci Adv., Sci. Rep., Comm. Biol, IJMS, JMB, JBC) or NMR (Biomol NMR Assign.). The publication track record is quite satisfactory considering the small size of the team and the involvement in the teaching. The number of funding is also quite significant (6), although only one has been obtained as coordinator. The team is also quite active on scientific communication to students and through the organisation of workshops.

Strengths and possibilities linked to the context

The well-recognised group leader until 31/12/2019 was involved in almost all the scientific production activity of the team with thirteen out of the fifteen total publications. The team is now led by a new PI, that develops the Galectin-related projects. The new PI was recipient of an ANR JCJC in 2016 focusing on the development of 'on-cell' NMR experiments to monitor binding of Galectins to physiological cell surface ligands. She has a good visibility (4 invited conferences, including an invited talk at Embo workshop, 2 ANR as participant, recipient of the Mourou Strickland award in 2020).

The team develops two main projects (on bacteriocin and galectins) but many collaborations internal to the Lism are also developed: on phage injection of *Vibrio cholerae* (with Team 3), on the study of a transmembrane helix from the type VI secretion system machinery (with Team 2 and Team 8) and on the periplasmic domain of a kinase involved in biofilm formation in *Pseudomonas aeruginosa* (with Team 5). They also have collaborations with other groups outside the Lism, in particular regarding the effect of the hydrostatic pressure on proteins from piezophilic microorganisms.

This is clearly a strength as it shows that team 6 is an undisputed local expert in the NMR field.

Overall, the track record is very good for a small team composed of one CNRS researcher, one assistant professor, one research engineer and one PhD student.

Collaborations have been developed with experts in glycan chemical synthesis (Cassia company), and in the development of specific isotope labelling for structural studies of carbohydrates.

Weaknesses and risks linked to the context

The publications of the new leader in terms of quantity (3 original articles) and quality are still limited although an article has been recently submitted.

Efforts should be made for securing grants, especially as PI and in attracting postdocs.

Publications with the highest impact factors are systematically from collaborative works, and often at an intermediate position in the co-authorship.

RECOMMENDATIONS TO THE TEAM

The committee encourages the PI to publish her recent results to strengthen her visibility. Overall, it is recommended that the new team leader consolidates her PI status with publications and grants in leader positions.

The team is highly dependent on NMR equipment located at the NMR platform of the IMM (FR 3479), or higher-field spectrometers thanks to the IR NMR national facility. Maintenance of a local equipment is crucial for their activity and significant investment is needed. The renewal of the equipment for NMR must be a priority to maintain a high level of research in this field.

Team 7: Lipolysis & Bacterial Pathogenicity

Name of the supervisor: Mr Stephane Canaan

THEMES OF THE TEAM

Lipid metabolism in mycobacteria with focus on lipolytic enzymes and development of inhibitors with potential therapeutic applications against tuberculosis

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

None. Team arrived in the Unit in 2018.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	2
Subtotal permanent personnel in active employment	5
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	2
Post-docs	0
PhD Students	3
Subtotal non-permanent personnel	5
Total	10

EVALUATION

Overall assessment of the team

Team 7 is an excellent mid-sized team with five permanent and two non-permanent members. The team studies lipid metabolism in mycobacteria with potential applications in tuberculosis; a major innovation is the development of two compounds with antituberculosis activities. Scientific production is excellent with 45 publications in journals of good to very good standard, including 1/3 of collaborative publications. The ratio of doctoral students (7)/researcher (6) is optimal. The team benefits from numerous funding (ANR, VLM over several consecutive years).

Strengths and possibilities linked to the context

This team is developing three main projects supervised by three principal investigators of the group. The converging point is to understand, at the molecular and physiological level, the lipid metabolism of Mycobacteria, its role in pathogenesis and its potential as a treatment target.

Team 7 has published a total of 45 articles (including 20 with members of the team as first or corresponding author) in journals of good to very good standard in its field of expertise (FEBS, Scientific reports, Plos pathogens, Infection and immunity, Embo). Journals are highly specialised or more general depending on the target audience. It is an excellent publication activity with regularity (5-9 each year). The team also obtained a patent for new fluorescent compounds capable of specifically labelling mycobacteria (in collaboration with the University of Missouri -St Louis).

The team is highly attractive with seven doctoral students and three postdocs during the reference period; 24 articles by the team include PhD students as co-authors. Two new members have joined the team in 2022 and the team has many national and international collaborations; this is indicative of its national and international recognition.

The team is involved in many reviewing and editing activities, which is also indicative of its recognition.

It has obtained many fundings (2 ANR as PI, Apex, grants from Vaincre la mucoviscidose for consecutive years).

The team contributes to scientific dissemination through the national 'science festival' event, and VLM meetings with families of patients.

Weaknesses and risks linked to the context

No weaknesses have been identified over the evaluation period, apart from, as mentioned by its self-assessment, the lack of European projects. But this is largely compensated by the many other fundings of the team

RECOMMENDATIONS TO THE TEAM

The team should maintain its excellent level of research activities in terms of publications, collaborations, PhD training.

Team 8: Assembly of bacterial multi-protein complexes

Name of the supervisor: Mr Eric Cascales

THEMES OF THE TEAM

Team 8 studies the architecture, the biogenesis and the mechanistic basis of protein transport across bacterial membranes through type VI secretion systems (T6SS) and type IX secretion systems (T9SS). This work follows two axes: the mechanisms of assembly of these machineries and the function of the secretion systems (characterisation of the secreted toxins and their activities in the target cell).

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

· *'the team should be strongly encouraged to apply to European sources in particular the ERC'*
 o the team has not applied to European or international grants. This is self-evaluated by the PI as a weakness in the Self-Assessment document (SAD) and, when questioned about this during the auditions, the PI stated that it was a deliberate intent to avoid the tedious effort and bureaucratic burden associated with submitting and managing European grants, in a context where all his projects are otherwise largely supported by national fundings.

· *'should consider developing collaborations with industry'*
 o the team declares that they have not yet established collaborations with industry but that they are actively working on it.

· *'an involvement in science fairs or interactions with school classes is encouraged'*
 o the team continues to be involved in science fairs and interact with school classes of various levels

· *'the two CR1s have excellent track records and should be encouraged to apply for the HDR as soon as possible'*
 o both chargés de recherche and the MCU have now defended their HDR.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	2
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	2
Subtotal permanent personnel in active employment	6
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	2
Post-docs	2
PhD Students	4
Subtotal non-permanent personnel	8
Total	14

EVALUATION

Overall assessment of the team

This is an outstanding team with original and innovative projects, that combines functional and structural approaches. Team 8 has an undisputed international reputation in the field of secretion systems. The scientific production of Team 8 is outstanding, with 51 publications in the most prestigious journals in the field. The team is also very active on scientific communication to students and to the general public. Over the evaluated period the team has been very successful in obtaining numerous important fundings from ANR, Amidex, FRM (overall, 12 fundings, half of them as coordinator).

Strengths and possibilities linked to the context

It is a relatively large team with fifteen people including six permanent staff (3 CNRS researchers, 1 MCU, 1 IR CNRS and 1 IE CNRS), two postdocs, two engineers on contract, four PhD students and one M2.

They combine a large set of classical techniques (molecular biology, bacterial genetics, biochemistry, fluorescence microscopy) with state-of-the-art structural biology techniques such as cryo-electron microscopy and cryo-electron tomography, native mass spectrometry and cross-link-coupled mass spectrometry. They also adapt or develop innovative methodologies (Apex2-dependent proximity biotinylation or *in vivo* NPP9-cross-linking coupled to mass spectrometry).

The team is internationally recognised in the field and this is illustrated by a large number of invitation to present in major conferences and to the invitation to write reviews or edit research topics in journals.

Their attractiveness is also highlighted by the overall number of collaborations (almost 75% of their research articles are in collaborative works), in particular *with top-notch structural biology groups (with the laboratories of Remi Fronzes, Laurent Terradot, Julia Chamot-Rooke, ...)*.

The team has supervised 6 PhD thesis with a very good associated publication record (3 - 10 articles per student).

Over the period under evaluation, Team 8 has published 51 articles (33 research articles, 8 reviews, 4 commentaries, 5 book chapters and one meeting report), 42 of which are signed as corresponding author. The average impact factor of the publication of the team is 9.6 (for research articles only).

Articles were published in the most prestigious journals in the field (Nature, Nature Microbiology, Cell, NAR, eLife, Nat. Comm.). The publications highlight important aspects of the molecular description of the functioning of secretion systems but also focus on methodological developments (Methods in Molecular Biology, Bioessays).

The team is also very active on scientific communication to students and general public, with interventions on public media (radio broadcasts, internet, popularisation magazines) and exhibitions in museums.

Over the evaluated period the team has been very successful in obtaining important fundings from the ANR, Amidex, or FRM (overall, they obtained twelve research fundings, most of them as coordinator).

Finally, Team 8 provides a very significant teaching duty with 450 hours/year in average for the whole team) and training courses of the Plinius PhD program.

Weaknesses and risks linked to the context

No weakness.

RECOMMENDATIONS TO THE TEAM

The committee recommends pursuing the excellent research and the mentoring of new generations of talented researchers. The national (and European) communities may benefit from their savoir-faire through the organisation of workshops or hands-on tutorials (Ecoles thématiques du CNRS, Ateliers Inserm, Embo courses...) Considering the biological targets studied, the team should consider collaborating with companies interested in antimicrobial drug development.

CONDUCT OF THE INTERVIEWS

Date

Start: 10 novembre 2022 à 1 h

End: 10 novembre 2022 à 1 h

Interview conducted: on-site or online

INTERVIEW SCHEDULE

8:15 Test Zoom connections (DU-CS)

8:20 Committee + CS (if needed)

Scientific sessions

8:30 - 8:40 Introduction/Presentation of the Committee members

8:40 – 9:05 Unit presentation by the DU (15' + 10' discussion)

9:10 – 10:30 4 Teams (10' + 10' discussion)

9:10-9:30	Team 1	<i>Pseudomonas aeruginosa</i> pathogenicity
9:30-9:50	Team 2	Dynamics and Assembly of membrane proteins
9:50-10:10	Team 3	Molecular transport across the bacterial cell envelope
10:10-10:30	Team 4	Virulence Nano-Macromolecular Machinosome

Break/debriefing committee (30')

11:00-12:30 4 Teams (10' + 10' discussion)

11:00-11:20	Team 5	Sensing environment & community lifestyle in <i>P. aeruginosa</i>
11:20-11:40	Team 6	NMR of molecular assemblies
11:40-12:00	Team 7	Lipolysis & Bacterial Pathogenicity
12:00-12:20	Team 8	Assembly of bacterial multi-protein complexes

Break/debriefing committee (30')

1 p.m.-2 p.m. **Lunch break/debriefing committee, if needed**

2 p.m.-2:30 p.m. **Meeting Committee with Supervising bodies (CNRS, Amu)**

Interviews

2:30 p.m.- 3 p.m. Meeting w/technical staff

3:15 p.m. – 3:45 p.m. Meeting w/students

4 p.m. – 4:30 p.m. Meeting w/researchers and EC (no team leaders) Debrief committee (15')

4:45 p.m.- Discussion Committee – DU Committee/Report briefing

PARTICULAR POINT TO BE MENTIONED

None

GENERAL OBSERVATIONS OF THE SUPERVISORS

Le Président de l'université

au

Département d'Évaluation de la recherche -
Hcéres

Objet : Observations de l'unité relatives au
rapport d'évaluation des experts Hcéres

N/Réf. : VPR/LS/AMS/CM – 23-07

Dossier suivi par : Cécile Merle

Tél : 04 13 94 95 90

cecile.merle@univ-amu.fr

Vos réf :

DER-PUR230023265 - LISM - Laboratoire d'ingénierie des systèmes macromoléculaires

Marseille, le jeudi 29 juin 2023

Madame, Monsieur,

Je fais suite au mail que vous nous avez adressé le 01/06/2023 dans lequel vous me communiquez le rapport d'évaluation Hcéres de l'Unité LISM - Laboratoire d'ingénierie des systèmes macromoléculaires

Comme demandé dans ledit mail, je vous fais part des observations de portée générale qui nous ont été remontées par l'unité :

First, the members of the unit would like to thank the various experts for the time that they have taken to examine the unit and the different teams that make up the LISM, and in the vast majority of the report I agree with the committee's analysis. Unfortunately, in the report on Team 1, **Pages 16-18** there are a considerable number of errors and interpretations inconsistent with those of the other teams.

- *The team should continue to collaborate to progress the work most effectively but ensure that they retain intellectual control of the projects.*

Collaboration is very active and productive, however, team members are not in leader positions in publications resulting from these collaborations.

The active collaborations have not resulted in a loss of intellectual control, and the position in collaborative publications as co-corresponding or penultimate authors is an indication of codirection and leadership, as pointed out for team 2 and indeed on the next page of the evaluation for the Plos pathogens article.

- *Team 1 thematic on *P. aeruginosa* virulence factors was effective to obtain grants from a charity association and ANR, but not from EU.*

The virulence factors thematic has been strongly funded throughout the period with multiple grants from charity associations, ANR, and Amidex, even though not from the EU.

- *However, team members were not in leader positions for publications in more recognised journals.*

This comment about team members not being in a leadership position in better journals is incomprehensible (and inconsistent with the assessment of other teams in the unit)

considering the last author and corresponding author positions of team members in Scientific Reports (twice), in Plos pathogens (twice) and Frontiers in Microbiology.

- Recommendation: Team 1 should also dedicate more effort to obtain additional national (or even European) grants to secure their functioning.

The team has been well funded for the entire period including from the ANR. This criticism is incoherent with that of other teams that have less, but adequate, funding and where no weakness was observed.

- The main recommendation of the committee is to increase the level of publications.

This recommendation of the committee for this team and no other team in the unit seems, on comparison, grossly unfair.

Taken together this collection of errors and the inconsistent treatment of this team is a serious deficiency and prejudices the report as a whole. This is unfortunate, as the remainder of the report, which is the vast majority (36/39 pages), is fair balanced and internally consistent.

Vous souhaitant bonne réception des présentes,

Je vous prie de croire, Madame, Monsieur, l'expression de mes respectueuses salutations.



Eric BERTON



The Hcéres' evaluation reports are available online:
www.hceres.fr

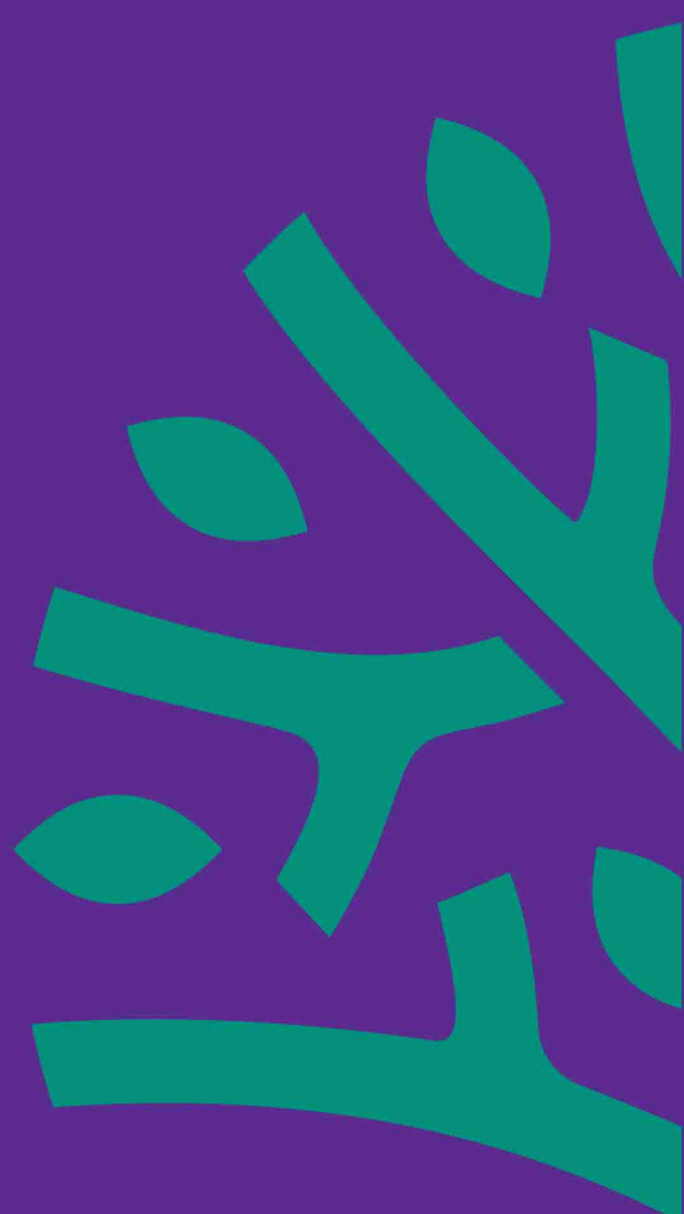
Evaluation of Universities and Schools

Evaluation of research units

Evaluation of the academic formations

Evaluation of the national research organisms

Evaluation and International accreditation



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