Research evaluation

EVALUATION REPORT OF THE UNIT

Citcom - Cibles thérapeutiques et conception de médicaments

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Université Paris Cité - UP Cité,
Centre national de la recherche scientifique - CNRS

EVALUATION CAMPAIGN 2023-2024
GROUP D

Rapport publié le 13/05/2024

High Council for evaluation of research and hihter education

In the name of the expert committee :

Isabelle Landrieu, Chairwoman of the committee

For the Hcéres :

Stéphane Le Bouler, acting president

Pursuant to articles R. 114-15 and R. 114-10 of the Research Code, the evaluation reports drawn up by the expert committees are signed by the chairmen of these committees and countersigned by the President of Hcéres.

To make the document easier to read, the names used in this report to designate functions, professions or responsibilities (expert, researcher, teacher-researcher, professor, lecturer, engineer, technician, director, doctoral student, etc.) are used in a generic sense and have a neutral value.

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:	Ms Isabelle Landrieu, CNRS - Centre national de la recherche scientifique, Lille
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Mr Didier Petitjean, UPC
Ms Christine Guillard, UPC
Ms Carine Giovannangeli, Inserm
Ms Claire de Marguerye, Inserm

CHARACTERISATION OF THE UNIT

- Name: Cibles thérapeutiques et conception de médicaments
- Acronym: Citcom
- Label and number: UMR8038 (ERL U1268)
- Number of team : 7
- Composition of the executive team: N. Leulliot: Director, I. Broutin : Deputy Director, P. Belmont : Deputy Director

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 Scientific project focuses on the analysis of therapeutic targets and on drug discovery. Four teams are covering expertise in biochemistry and structural biology and three teams bring expertise in medicinal chemistry, toxicology and analytical chemistry, chemistry of natural products. The Unit has a strong translational component provided by the chemistry teams. At the fundamental level, the structural biology teams decipher molecular mechanisms involving protein/RNA, protein/protein or protein/membrane interactions with an impact on multiple human diseases, mainly in the infectiology, cancer and genetic disease fields.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

Citcom belongs to the Faculté de Santé (Faculty of Health) of Paris Cité University, CNRS being the other supervising body of the laboratory. The laboratory is part of the Biology and Chemistry institutes of the CNRS. Citcom originates from merging LCRB (Laboratory of Crystallography and Biological NMR) and Comete (Organic Chemistry, Toxicological and Environmental Extraction) in a single Unit in 2017. Team 6 is an Equipe Mixte de Recherche with Inserm as an additional supervising body. The laboratory is hosted by the Faculty of Health, within the pharmacy buildings.

RESEARCH ENVIRONMENT OF THE UNIT

The laboratory benefits from the mixed service unit (UMS) from the health faculty and hosts in addition two platforms, 'Mass spectrometry-metabolomics-lipidomics' and 'safety toxicology'. The laboratory is affiliated to Ecole Doctorale 563 – Médicament, Toxicologie, Chimie, Imagerie (MTCI) and Citcom members are represented in its managing council.
Citcom is a Paris Cité University Chemistry Research Federation (FédCUP) member, which gathers around 300 chemists for scientific animation.
The laboratory is part of the EUR MCC (Medicine: from conception to clinical application), with team 6 leader as coordinator.
The laboratory has benefitted from the programme PIA 'investissement d'avenir' by the idex, Equipex Cacsice and CPER Pharm-EM grants.
Translational research projects are conducted with Hospital Cochin and Hospital 15–20.
Yslab company is hosted in the laboratory facilities.

UNIT WORKFORCE: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	13
Maîtres de conférences et assimilés	38
Directeurs de recherche et assimilés	5
Chargés de recherche et assimilés	5
Personnels d'appui à la recherche	30
Sous-total personnels permanents en activité	**91**
Enseignants-chercheurs et chercheurs non permanents et assimilés	7
Personnels d'appui non permanents	0
Post-doctorants	1
Doctorants	29
Sous-total personnels non permanents en activité	**37**
Total personnels	**128**

DISTRIBUTION OF THE UNIT'S PERMANENTS BY EMPLOYER: in physical persons at 31/12/2022. Non-tutorship employers are grouped under the heading 'others'.

Nom de l'employeur	EC	C	PAR
UNIVERSITÉ PARIS-CITÉ	51	0	15
CNRS	0	8	12
AUTRES	0	2	3
Total personnels	**51**	**10**	**30**

GLOBAL ASSESSMENT

The Citcom laboratory has excellent visibility stemming from its rather unique position at the national level of developing basic research, within the Faculty of Pharmacy of Paris-Cité University, with a biology/chemistry interface. The global quality of Citcom scientific production is very good to excellent. The Citcom lab generated about 400 publications in international peer-reviewed journals. Publications reflected the laboratory expertise in biochemistry, structural biology, RNA structure and biology, analytical chemistry, chemistry of natural products, medicinal chemistry and toxicology disciplinary fields. Team members have published their research in journals ranging from specialised but well-regarded journals (e.g. BBA, Sci. rep, PlosOne) to high visibility disciplinary journals (e.g. Nucleic Acids Res., J. Med.Chem., ACS Chem Biol., Anal. Chem…) or multidisciplinary journals (Angew. Chem., Nat. Comm., Cur Opinion Chem…). Interestingly, the experimental approaches are strongly supported by in-silico modelling across all the disciplinary fields (RNA 2D/3D structure prediction, DFT calculations to facilitate organic synthesis, chemo- and bioinformatics for chemical and metabolomic analysis…).
Citcom laboratory has demonstrated an outstanding capacity to attract funding though competitive calls to allow its project to proceed in the best conditions, with 33 ANR/1 INCA/2 Anses granted ongoing funding during the period, including thirteen projects as coordinators. Notably, the Unit has demonstrated its capacity to improve its infrastructure by coordinating a large CPER grant (Pharm-EM) and the Equipex Cacscise that will ensure the installation of a much-needed cutting-edge cryo-electron microscope. The laboratory projects have been strongly supported by the idex (14 funding), including a chair. Disappointingly, most of the offices and laboratory spaces are in poor states, causing concerns about the safety and well-being of the laboratory members', who must be commended for their dedication for advancing their research in such conditions. Some renovations are anticipated that should partially improve the conditions and the committee strongly supports that this effort has to be maintained.

The laboratory has also hosted 70 PhD-level students, demonstrating the attractiveness of its research project, although the distribution of this training among the teams is uneven. The expertise of Unit members was sought in a number of institutional governance bodies and scientific committees in France. Unit members were also very well represented in learned societies (e.g. SFBBM, société de chimie thérapeutique) and in three GDRs (e.g. Cosm'actifs), in managing positions from which they participated actively in the organisation of national scientific events. At the international level, several initiatives are to be commended, such as a Lia Andes with Brazil exiting since 2012. A European Rise project (Exandas) involving a large consortium dedicated to natural compound chemistry has been pursued during the period. Bilateral relationships have been formalised by Partenariat Huber Curien (PHC Tassili, Balaton) and lab members have been involved in two COST actions. Considering that the period was not the most auspicious to develop international collaborations (Pandemia, Reforming the Pharm.D. curriculum), the committee still believe that the laboratory has the potential to increase its international standing in the coming years, for example, by attending more international conferences on their topics of expertise.

A major goal of the laboratory is drug discovery and its research outcomes are directly connected with pharmaceutical innovation and translational aspects. In this context, the laboratory has managed excellent exploitation of its expertise, with five Cifre fellowships ensuring close collaboration with companies and five patent depositions that set the ground for future exploitation. Innovation projects were supported by innovation agencies (e.g. SATT/University – 1). The committee believes that given the potential provided by its drug-oriented program, scientific results could be more broadly exploited including increased interactions with the SATT or other maturation offices and/or with large pharmaceutical companies.

Lab members have disseminated their knowledge by outstandingly contributing to teaching at the Pharmacy Faculty of Paris Cité. They have been in contact with the public by e.g. taking the opportunity to join actions such as lectures targeting the general public, broadcasts (France Culture interview), and visits to elementary schools and open-doors for college and lycée students or the faculty open day. They have also served on the board of patient associations such as La Ligue contre le Cancer.

DETAILED EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Securing international funding (ERC grants, IMI consortia, ITN calls, etc.)
The Unit has not been able to secure European funding during the period (one project Rise has been ongoing as a partner). However, encouraging actions have been taken such as participation to two COST actions in managing positions and two bilateral PHC, which could seed larger international projects.
T**he laboratory is dispersed over the campus of the faculty/lack of equipment and insalubrious facilities** The Plan Campus has been abandoned in its original form and there is no known new plan. A rehabilitation of one of the buildings is considered. In summary, no short-term solution has yet been found. Regarding equipment, a project for large equipment acquisition is ongoing and funding is secured but doubts remain on the associated hosting building funding.
The relatively high turnover of personnel asks for a strategy to retain and recruit (new) staff:
New Inserm, CNRS and Paris-Cité researchers have been attracted through mobility
The review committee advises designing a transition plan for the merger, for which it is recommended.
To call upon external expertise
A SAB was consulted on some specific points (e.g. recruitment of a new PI for Team 4) and two on-site visits were organised.
Encourage transversal project
There was no top-down action regarding this kind of multidisciplinary project but at least at the level of funding, a number of granted projects have been multidisciplinary (Biology-Chemistry)

B – EVALUATION AREAS

Considering the references defined in the unit's evaluation guidelines, the committee ensures that a distinction is made on the outstanding elements for strengths or weaknesses. Each point is documented by observable facts including the elements from the portfolio. The committee assesses if the unit's results are consistent with its activity profile.

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

Assessment on the scientific objectives of the unit

The multidisciplinary and translational environment of the laboratory is a strong opportunity to reach its drug discovery goals.

Assessment on the unit's resources

The Unit has shown an exceptional capacity to attract funding to acquire and maintain infrastructure, including the acquisition of a state-of-the-art cryo-EM microscope. A very large range of equipment is available for the laboratory members. The laboratory and office spaces do not meet the expected standards for a modern research facility.

Assessment on the functioning of the unit

The laboratory follows the rules imposed by its supervising bodies, but there is room for improvement in internal communication, which is strongly impaired by the dispersion of Citcom staff around the building, and data management, which does not benefit from internal or external IT support. The laboratory strives to support all team activities by funding its major equipment maintenance. The current administrative support is insufficient, impacting all Citcom staff activities.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

The Scientific project of the laboratory focuses on drug discovery and benefits from research conducted at the Biology and Chemistry Interface, covering fundamental science, pharmaceutical innovation and translational aspects. The laboratory strongly benefits from multidisciplinary expertise in structural biology, medicinal chemistry, biochemistry, genomics, proteomics, metabolomics, and chemo-informatics. Research projects cover a wide variety of pathologies (cancer, infections, genetic diseases, etc.) and biomolecule targets.
Staff members benefit from seminars mainly at the Pharmacy Faculty where external members are invited to share their work.
The laboratory has received the support of an advisory board to shape his project and to mentor the integration of the teams (two visits).

Weaknesses and risks linked to the context

The range of covered topics (targets) is very broad and complementarity is not sufficiently demonstrated, by an overarching project, for example. The laboratory internal seminars have been discontinued.

2/ The unit has resources adapted to its activity profile and research environment, and makes use of them.

Strengths and possibilities linked to the context

Funding by the PIA Equipex Cacsice and CPER Pharm-EM grants will enable the Unit to acquire a state-of-the-art Cryo-Electron microscope for single particle structural analysis, cryo-tomo and Micro-ED. A Helium recycling project involving the various Paris-Cité laboratories will help to sustain the NMR infrastructure.
The' Mass Spectrometry-Metabolomics-Lipidomics' (SM2L) platform is managed by Team 5 and is certified by Paris-cité University. An LC-HRMS/MS equipment is available within this platform for a fee. The Predictive cellular toxicology and health safety platform is also managed by Team 5 and is certified by Paris-Cité University. Importantly, this platform has the expertise to implement standardised assays for safety evaluation. In addition, the laboratory has organised a number of internal core facilities, including 300, 400 and 600 MHz NMR spectrometers, the latter being equipped with a cryo-probe. One of the core facilities is collectively managed and benefits the 4 structural biology teams 1 to 4. Analytical and Preparative Chromatography facility managed by Team 6 benefits to the internal teams but is also used for external training.
The unit has recruited a dedicated staff to manage the chemical compound collection.
The recurring funding is used for maintenance and running costs of shared consumables, both for chemistry and biology and the maintenance and running costs of the NMR spectrometers. About 40% of the recurring funds are equally divided between the teams. Medium size equipment is acquired yearly with this budget (*e.g.* -80% congelator). The Unit also benefits from the 2% overhead and management costs of the ANR project.

Weaknesses and risks linked to the context

The hosting, maintenance and staffing of such a large piece of equipment as a cryo-electron microscope for single particle analysis will need to be carefully managed to sustain its use and take full advantage of this opportunity. In this respect, the involvement of experienced staff from the Institut Pasteur is a positive initiative. The time-scale of the hosting building development is a concern.
The offices and laboratory spaces are in such a poor state that they impact the well-being and security of Citcom staff. The laboratory is dispersed around the building inducing risks related to isolated work, movements of chemical products and numerous stairs. Dysfunction of part of the hoods is regularly suffered, limiting work and causing security risks. Proper storage of chemical compounds is lacking and induces a strong security risk. Offices are overflowing with staff. The SST staff is insufficiently advertised. Citcom staff can only be commended for their resilience in pursuing their projects in these conditions. On a positive note, one team will benefit from renovated spaces in the short-term.

3/ The unit's practices comply with the rules and directives laid down by its supervisory bodies in terms of human resources management, safety, the environment, ethical protocols and the protection of data and scientific heritage.

Strengths and possibilities linked to the context

The Unit follows the rules set out by CNRS and UPC for recruitment, according to their HRS4R procedures. Assistants de prevention are appointed and a Unit budget is specifically dedicated to security improvement. There is a dedicated committee for safety and well-being management headed by two designated AP with an advisory role towards the Unit director. The Unit has a 'conseil de laboratoire'.
AP also informed newly incoming staff of the general risks and good practices. Training on specific equipment is provided. Unit members are informed about good IT practices thanks to procedure guidelines described in the 'règlement intérieur'. Training on IT risks is provided for incoming staff.

Weaknesses and risks linked to the context

Poor data management (the Unit is lacking a backup server) and lack of data storage are concerns and on a lower level, of e-lab books.
The internal 'gazette' to keep the staff members informed of institutional and internal scientific news was appreciated and was discontinued because the editor (who is in charge of the administrative part of the Unit!) is overworked. Information regarding decisions taken at the level of the managing committee is insufficiently spread and there is a lack of visibility on the major strategic orientations of the laboratory for its staff. Some procedures are in place to welcome incoming staff (communication of the 'charte du laboratoire', NEO) but there is room for improvement because the initiative mainly relies on the teams, with variable outcomes.
There is a current weakness in the administrative support due to staff shortage, which impacts the whole laboratory.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The expertise of the Unit members at the National level is outstanding as shown by their participation to multiple networking activities and contributions to scientific committees, GDRs and learned societies. The ability of the Unit members to fund their project through application to highly competitive calls (ANR) at the national level is outstanding. Participation to COST action at the European level is a promising step to improve the Unit visibility at the European level towards securing large European grants.

1/ The unit has an attractive scientific reputation and is part of the European research area.

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

3/ The unit is attractive through its success in competitive calls for projects.

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

Strengths and possibilities

The Unit has an excellent support of its supervising bodies. It has obtained a 'chair de professor junior' at UPC supported by the idex leading to the recruitment of a professor in Team 6 following a competitive call. Team 6 has received an Inserm label. The laboratory has been strongly supported by the idex initiative (3 PhD fellowships, 10 funded emerging projects), a CPER and the Equipex Cacscise. The CPER and Equipex permitted the

improvement and/or renewal of the unit equipment, increasing its attractiveness for the next period. Notably, a high-resolution cryo-microscope for single particle analysis will be available.

The Unit has been excellent at attracting new funding. Numerous grants have been obtained by team members, totalling ten Meuros for the five-year period. Altogether, 33 ANR/1 INCA/2 Anses funding were granted to team members, including thirteen as coordinators and 30 newly obtained during the period, demonstrating in these very competitive calls the attractiveness of the research conducted in the Unit and capacity of team members to lead the field. The seven funded projects in 2022 offer an excellent starting point to engage in the next period.

One grant was obtained at the European Level as partner during the previous period H2020-MSCA-Rise-2015 and project Exandas has continued until 2020. Two campus France PHC (Balaton and Tassili) have sustained bilateral international collaboration. Additionally, coordination of the COST action Eutopia and participation to the COST action CM 1407 (from Natural Product chemistry to drug discovery) management committee (as substitute) are together very encouraging steps to participation to large european network. The laboratory was also part of the international laboratory LIA Andes (2014–2022) with the Catholic University of Chili.

New researchers have (or will shortly) joined the Unit on mobility. Leadership of Team 4 has been renewed following an external competitive recruitment.

Staff members have occupied positions in various boards of French learned societies (e.g. SFBBM), at the Pharmacy Academy and in Scientific Council of charities (e.g. La Ligue contre le Cancer, Fondation Pierre Fabre). The Unit partcipates to three GDRs (Cosm'actifs, i-npchem, …) contributing to the national visibility of its research. The Unit is also represented at the International level in networking activities (e.g. French-Brazilian Natural Product Network, Phytochemical society of Europe) and one staff is a member of the Swiss pharmaceutical science academy.

Staff members have actively contributed to the organisation of scientific meetings, mainly on the local and national levels in the context of learned societies (SFBBM, Société de chimie thérapeutique), including actions targeted at young researchers (young researcher meetings).
Expertise of Unit staff has been provided in many instances to evaluation bodies (ANR, Hcéres) and their recommendations seek by Anses (Vigilance Toxines Naturelles, « Médecine traditionnelle chinoise »…). Staff members have also contributed to multiple steering bodies from the Pharmacy Faculty to the University and the CNU.
70 PhD students have joined the laboratory during the period (9 on international mobility, 26 in Team 6), corresponding to a massive investment of the laboratory teams in young researcher funding and training. To achieve this very high level of training, funding of PhDs has been diversified, mainly through doctoral contracts, but also using ANR & idex grants (3 fellowships), five Cifre fellowships, twelve fellowships from abroad, one from EU and one from an international fellowship.

Weaknesses and risks linked to the context for the four references above

The offices and laboratory spaces are in poor states strongly impacting the attractiveness of the Unit.
The Citcom website is insufficiently maintained and updated.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The global quality of Citcom's scientific production is very good to excellent, reflecting the multiple expertise developed in the laboratory through the diversity of journals.

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

2/ The unit's scientific production is proportionate to its research potential and properly shared out between its personnel.

3/ The scientific production of the unit complies with the principles of research integrity, ethics and open science. It complies with the directives applicable in this field.

Strengths and possibilities

The Citcom lab generated about 400 publications in international peer-reviewed journals. Publications reflected the laboratory expertise in biochemistry, structural biology, RNA structure and biology, analytical chemistry, chemistry of natural products, medicinal chemistry and toxicology disciplinary fields. Team members have published their research in journals ranging from specialised but well-regarded journals (e.g. BBA, Sci. rep, PlosOne) to high visibility disciplinary journals (e.g. Nucleic Acids Res., J. Med.Chem., ACS Chem Biol., Anal. Chem…) or multidisciplinary journals (Angew. Chem., Nat. Comm., Cur Opinion Chem…). Interestingly, the experimental approaches are strongly supported by in-silico modelling across all the disciplinary fields such as RNA 2D/3D structure model prediction (De Bisschop et al. 2021, Non-Coding RNA), DFT calculations to facilitate organic synthesis (Norsikian et al. 2020, Angewandte Chem.), chemo- and bioinformatics for chemical and metabolomic analysis (e.g. Magny et al. 2020, Metabolites). Importantly, the computing approaches in these studies are very well embedded in complementary experiments of (bio) chemistry.

Weaknesses and risks linked to the context for the three references above

Most of the publications are in specialised journals, limiting the visibility of the laboratory research.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

A major goal of the laboratory is drug discovery and its research outcomes are in direct connections with pharmaceutical innovation and translational aspects. The committee believes that given the potential provided by its drug-oriented program, scientific results could be more broadly exploited. Lab members have disseminated their knowledge by an outstanding contribution to teaching at the Pharmacy Faculty of Paris Cité.

1/ The unit stands out for the quality and the amount of its interactions with the non-academic world.

2/ The unit develops products for the cultural, economic and social world.

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

Strengths and possibilities

The drug discovery objectives of the laboratory and translational activities are to the benefit of a large public.
The laboratory has benefited from five Cifre PhD fellowships.
Team 5 hosts two members of Yslab company and has a joined research project. Interactions have also been ongoing with the start-up Erganeo.
Research and innovation funding were obtained from SERVIER for the chemical synthesis of specific compounds and for the NCS Tox Unitis project.
Expertise was provided regarding compounds toxicity (essential oils).
Innovation projects were supported by Inserm transfert (1), SATT/University (1) and the Fonds regional pour l'innovation (1).
The Unit has filed five patents. One patent covers a placental toxicity assay that was highlighted of high interest at the European level.
The compounds inhibiting caspase 2 and their use in treating inflammation have resulted in two patents and a maturation project supported by SATT/University and the start-up Erganeo. The project was awarded at the very competitive innovation challenge i-lab (2022). The start-up IPCure resulted from this innovation project.

Unit members share their expertise by their strong commitment to teaching at the University

Weaknesses and risks linked to the context

Innovation commitment is excellent but given the potential provided by the drug-oriented program of the laboratory, it could be more broadly exploited including by increasing interactions with the SATT and/or large pharmaceutical companies.

ANALYSIS OF THE UNIT'S TRAJECTORY

One objective of the Unit is to improve the infrastructure/equipment available to the Unit team that could support various research lines in direct relation with the Unit objective of drug discovery. The analysis of the needs is well thought and complement well the existing facilities, with additional support expected for in-silico calculations, reinforce the toxicology platform, install medium-scale screening facilities and finally improve the chemical library to better exploit the potential of the compounds synthesised and analysed in the laboratory. This indeed would strengthen the attractiveness of the laboratory and would have a positive impact on research in the laboratory but also beyond its walls, given external access or sharing of compounds.

New team(s) or researchers might join the laboratory for the next period, which represents both risks and opportunities. That should be carefully examined and additional external advice might be of use. A collective reflection on the laboratory objective(s) and how it would be strengthened by new expertise arrival is very important.

RECOMMENDATIONS TO THE UNIT

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

The scientific exchanges within the Unit could be reactivated as it seems that they have suffered since the years of lockdown and have never regained previous levels. The laboratory will continue its efforts to enable scientific and human exchanges between the teams, ensuring the development of interdisciplinary synergies. The committee recommends to the younger researchers within the laboratory, who seem to be a positive and cohesive force within the Unit, to take some initiatives to enforce scientific exchanges with the help of the Citcom direction. The laboratory council would benefit from a clear agenda and minutes of the meeting and in a general manner, spreading of strategic decisions should be increased. The new members of the laboratory would benefit from a formal introduction to their workplace and environment, beyond the hand-on that they receive in the teams.
Administrative management within the Unit should be improved, hopefully by attracting an additional person. The committee hopes that the coming years will bring improvement in the working conditions and security of Citcom members and can only recommend that they continue their efforts of advocating for change.

Recommendations regarding the Evaluation Area 2: Attractiveness

The committee believes that the laboratory has the potential to increase its international standing in the coming years, by for example attending more international conferences on their topics of expertise. The coherent evolution towards fewer themes would improve the visibility of the laboratory, beyond its excellent technical skills.

Recommendations regarding Evaluation Area 3: Scientific Production

The laboratory can draw on its interdisciplinary resources to increase its visibility in journals of interest to a broader scientific community. The committee recommends increasing international collaboration with leading laboratories to support the laboratory standing and bring-in new expertise.

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

The committee believes that given the potential provided by its drug-oriented program, scientific results could be more broadly exploited including by increasing interactions with the SATT or other maturation offices and/or with large pharmaceutical companies.

TEAM-BY-TEAM OR THEME ASSESSMENT

Team 1: Molecular RNA machineries and human pathologies

Name of the supervisor: Mr. Nicolas Leulliot

THEMES OF THE TEAM

The main theme of the team is the structural study of ribonucleoproteins (RNPs) biogenesis (theme 1) using a combination of biochemistry, X-ray crystallography and more recently cryo-electron microscopy and single-particle analysis. The team expertise in structural biochemistry is also used in various collaborative projects, including the study of protein-inhibitor complexes (theme 2), the structure elucidation of small chemical compounds (theme 3) and the structure-function analysis of disease-related mutations (theme 4).

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The first series of recommendations was about publication/collaboration strategies, European grant applications and PhD student publications. The team did not obtain any European grant during the evaluated period. Except for the numerous collaborative studies using high-pressure crystallography (with T. Prangé), no article in the context of an international collaboration was published during the evaluated period. Only one article on the main theme of the team (RNPs) was published during the evaluated period (NAR, 2017). Two preprint papers are mentioned but not submitted to bioRxiv. It also seems that the publication of the main paper of the PhD students is happening some years after the actual defence.

The second recommendation was about attracting young CNRS and Inserm scientists in the team: one Inserm scientist left the team and no new scientists joined the team in the evaluated period; the main reason for this lack of attractiveness might be the bad state and poor quality of the building and lab spaces.

In the third recommendation, the committee strongly suggested to the team to focus on RNPs; the group continued its work on RNP biology (the three PhD projects of the evaluated period were focused on ribosome biogenesis, theme 1) but the team kept its activities in the three other themes as they provided the vast majority of the publications during the evaluated period.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	6
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	**10**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	1
Sous-total personnels non permanents en activité	**2**
Total personnels	**12**

EVALUATION

Overall assessment of the team

The team really took advantage of the merging of the two previous labs to foster new projects with many teams in the unit and to secure important funding to run all its projects for the evaluated period. The biggest achievement is definitely the future acquisition and installation of a cryo-electron microscope: although exciting and promising, it could be an extremely challenging operation for the team (and the unit itself). The overall scientific production of the team is good to very good.
The main theme of the team, RNPs biogenesis, is extremely competitive, and the efforts put in this subject by the team over the last years still need to be confirmed.

Strengths and possibilities linked to the context

The team built strong interactions with team 5, 6 and 7 in the context of the merging of the two labs that created the current unit, allowing very 'hot' subjects to be tackled (novel cancer therapies targeting ribosome biogenesis) and dedicated grants to be awarded (3 ANR and 1 INCA for ~500k€) during the evaluated period.
The members of the team are extremely involved in many aspects of the scientific life at the local, national and international levels, through their involvement in science societies (SFBBM, FEBS), university responsibilities (teaching, management, counsels) and expert/reviewing missions. Indeed, the team organised the SFBBM annual congress in 2021 with more than 200 participants, and the teaching members of the team have been awarded many competitive education innovation call projects in the last years.
In collaboration with the Nanoimagerie core of Institut Pasteur, the team secured a budget (through Equipex, CPER, Inserm and UPC) to acquire and set up a cryo-electron microscope within the unit. This technology became absolutely essential for many structural biology projects and it will undoubtedly benefit many projects within the unit, and being only the third one being installed in Paris, that will make the laboratory a major player in the field at the local and national level. A permanent staff (IR) dedicated to the instrument has already been recruited and a suitable room is currently being renovated to host the microscope for a delivery and installation by the end of the year.
The team has established several partnerships with economic actors, through for instance an AIMA grant to study the feasibility of human telomerase on a pre-industrial scale in the context of the production of a universal cancer vaccine; this project is to be continued via an ANR project currently submitted. The team is also dedicated to promote education, science and healthcare to the general public: 'Pint of Science' festival, pharmacy school open-door events, RIGOLE workshop, communications in newspapers against fake news…

Weaknesses and risks linked to the context

The team is composed of six permanent researchers with heavy teaching duties on top of the admin ones, limiting their time for actual research and mentoring. The lack of HDR within the team members is also a problem as it limits the number of PhD students that can be hosted by the team.
The vast majority of the 42 papers published during the evaluated period are related to the studies of small molecules by X-ray crystallography, with a scientific production unevenly shared among the team members. The main in-house project on ribosome biogenesis has not been very productive during the evaluated period and the related studies (two preprints mentioned, including one from a PhD student) seem to be difficult to finalise.

Analysis of the team's trajectory

The team aims to continue working on small molecular crystallography and protein-inhibitor structural studies through various collaborations.
The team also presents a very exciting and ambitious research program on RNPs and more specifically on RNA helicases mechanism deciphering, ribosome biogenesis and p53 pathway as a target for cancer therapies, including the study of small molecules to activate the tumour suppressor p53, using in vitro screening assays, cryo-EM, fragment-based approaches with X-ray crystallography, etc... In this context, the team already established various collaborations with teams within or outside the unit to tackle these challenges, and also presented some solid preliminary results validating the feasibility of the projects and the strategies proposed.
The team also insists on the fact that cryo-EM will become one of its main tools in its future projects as many members already have a good knowledge of the SPA approaches for structural studies of their complexes of interest.

In a very sensible and wise view, they also propose to implement and develop micro-electron diffraction to study the structure of small chemical compounds rebellious to classical X-ray diffraction approaches. This will definitely be extremely complimentary with the current expertise of the team and an excellent added value for the coming cryo-EM platform and of great interest for the other chemistry teams of the unit.

RECOMMENDATIONS TO THE TEAM

As already suggested during the previous evaluation, the committee strongly encourages the team to focus more its research on RNPs biology (RNA helicases and ribosome biogenesis), and to have a better balance in terms of publications between the different research themes.

The local and national visibility of the team is excellent and the committee recommends continuing being implicated in science societies and university departments despite the obvious heavy teaching burden. The experts suggest to strengthen the international visibility of the team by setting up new collaborations, applying to European grants and participating to international conferences ('Ribosome Synthesis', 'Ribosomes Meeting', 'Annual RNA society Meeting', etc.).

To valorise the work of the PhD students (and postdoctoral fellows) and to increase the visibility of the team in the RNPs field, the committee strongly encourages the team to deposit its manuscripts on a preprint server (bioRxiv) and to increase its efforts to finalise their publication.

The addition of cryo-EM capabilities is fantastic news for the unit; the committee advises the team (and the unit) to carefully prepare the installation and running of such a machine: room specification, booking rules, training, sustainable financial models, etc. The team is also strongly advised to be part of the local and national cryo-EM community.

Team 2: Signalling and membrane transport group

Name of the supervisor: Ms. Isabelle Broutin-L'hermite

THEMES OF THE TEAM

The team specialises in structural biology of membrane proteins. Their main project concerns systems linked to antibiotic resistance, in particular the study of the assembly, function, physiological role and regulation of the expression of bacterial RND efflux pumps in the opportunistic bacterium *P. aeruginosa*. Two other projects are developed, a theme on angiogenesis (human VGEF receptors), and the recent development of tools based on DNA-origami.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The position of the team in external collaborations is not always strong enough.
The PI is co-corresponding author of Nat Com. 2020 (portfolio item 1) acknowledging the utmost importance of know-how on the biochemistry of their systems for cryo-EM structure resolution.
The team should enhance participation to international congresses and strengthen collaborations with international teams. The team participated in international congresses (7 communications, 5 posters) and applied to a European funding.
Acquiring progressively the know-how in electron microscopy should also be considered. Three team members trained in EM data acquisition and processing.
As far as industry is concerned, lack of interactions is a weakness for the team.
The team has not yet established collaborations with industry. The PI became an active member of the SFM to develop networks.
The number of PhD students is currently low. It was higher in the past: three PhD students (2 defended) were hosted, a number still lower than it used to, but coherent with the number of HDR (4 until 12/19, now 3).
The size of the team and the departure of one of the researchers, who will continue his own project on efflux pumps in a neighbouring institute, are weak points.
The team continues the initiated project with him through collaboration. The staff further evolved with two departures in 2019 (1 CR, 1 IR) and two recruitments in 2020:one MCU, one AI CNRS, bringing their respective expertise (DNA-origami, nanodiscs).

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	4
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**8**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	1
Sous-total personnels non permanents en activité	**2**
Total personnels	**10**

EVALUATION

Overall assessment of the team

The team has an excellent recognition for its work on efflux pumps and membrane protein structural studies. Its excellent visibility and dynamism are attested by its involvement in scientific societies, organisation of congresses and strong networks. Scientific production was very good to excellent, especially for a small team with heavy teaching duties. A major achievement on MexAB/OprM pump operation was acknowledged by a high visibility article.
Staff evolution may have had an impact on the team, limited by the focus of the team on the pump thematic and recruitment of two new members.

Strengths and possibilities linked to the context

The team is renowned for its work on structural study of membrane proteins and antibiotic resistance mechanisms, in particular efflux pumps in P. aeruginosa. The team aims to understand the assembly, the function and expression of these pumps as a first step to develop strategies to block them or their expression. Functional and structural studies by cryo-EM of MexB and of the whole MexAB-OprM efflux pump have led to a major advance in our understanding of how the pump works to extrude drugs (Nat Com 2020, portfolio item 1). The development of biological tools based on origami DNA technique by the new recruited EC could further help the characterisation of these pumps (quality sample improvement for cryo-EM, pump reconstitution). A PAR CNRS with expertise on nanodiscs also joined the team in 2020. Most of the team members thus now joined their forces for the development of this research axis. Another eukaryotic project on VEGFR, led by an EC (collab. with Team 6) has important fallouts in clinic.
Production of the team (24 publications) is very good to excellent considering its size, the absence of permanent PAR support before 12/2020, heavy teaching duties and university responsibilities. In particular, several team members were in charge of the setting up of the 'Health teaching reform' at the Pharmacy faculty (portfolio item 3). Articles were published in peer-reviewed journals, from specialised (BBA, AAC, Sci. rep, Plos One, Frontiers, IJMS, etc.) to broad audience-high visibility (Nat Comm) journals. The publication rate is relatively well distributed according to themes and project leaders, with most of the publication related to antibiotic resistance (13). The recently joining MCU has an excellent publication record during this period (7 including 1 Nat Comm), but yet only one review is affiliated to Citcom. The project on VEGFR led to very good and regular publications (4). Most publications are local or national collaborative work with several teams, reflecting the strong network established by the team. Two team members were involved in the edition of a special issue for 'Antibiotics' open access journal (portfolio item 2).
The recognition of the team has been outstanding, especially at the national level. As members of the scientific board of several French Societies thematic groups/sections (SFM, GEM, SFBBM, etc) the team was involved in the organisation of seven scientific events (*e.g.* portfolio item 4). Their strong networks (*e.g.*, Pseudomonas and Membrane protein 'communities') favour collaborative work and led to the acquisition of two ANR grants as partners. Together with an ongoing ANR, two VLM grants and idex obtained in the period, the team secured adequate money for staff hiring (1 PAR, 2 PhD) and running costs.
The scientific reputation of the team is also attested by its participation in PhD or HDR jury panels, recruitment committees for university positions or grants evaluation.

Weaknesses and risks linked to the context

The team is implicated in scientific animation (groupe d'animation scientifique AnimPharma de la Faculté de Pharmacie Université Paris Cité), organising seminars and specific events, that link the different local and Ile de France scientific sites and students. However, as most team projects are related to major public health problems, the team should find more opportunities to popularise science to the general public.

Analysis of the team's trajectory

The projects of the team are very clear, in continuity and also interesting new and exciting goals, such as the development of efflux pumps inhibitors.
The first axe on RND efflux pumps involves most members of the team. In continuation of their work and achievements on MexAB-OprM, the team proposes to solve the structure of another pump able to efflux aminoglycosides largely used in clinics, which they can produce well now, using nanodiscs for membrane protein reconstitution and cryo-EM. They will continue promising ongoing projects on transcriptional regulators (a subject further extended to other pathogens, with two new collaborations).

Importantly, they aim to develop specific inhibitors of the transporters and pump assembly, such as peptidomimetics targeting protein/protein interfaces, through a collaborative work with chemists (Team 7), modellers, microbiologists and toxicologists. They also aim to develop screening tests for molecules restoring antibiotics sensibility, optimised for P. aeruginosa.
The second axe is the development of antiangiogenic molecules targeting the VEGF signalling, with several developed molecules having promising fallouts in clinic.
The third axe concerns the development of tools using DNA origami that are very interesting per se and could also be very useful for the projects presented in axe 1.

RECOMMENDATIONS TO THE TEAM

The team is rather small with most members having heavy teaching duties and responsibilities at the university. If the management of the PhD students seems to be adequate, their number may be limited by the number of HDR in the team. The evaluating committee recommends to the team to set up the required conditions for the MCU to obtain their HDR: students mentoring, corresponding authorship, …
The team has an excellent national visibility and networks through their implication in science societies and GDR that should be maintained. The committee recommends continuing their efforts to reinforce the international visibility of the team.
Publications in fast-track journals (MDPI…) should be taken with caution.
The team should consider developing collaborations with industry to capitalise on the potential medical benefits of their work.

Team 3: Molecular mechanisms of viral RNA translation

Name of the supervisor: Mr. Bruno Sargueil

THEMES OF THE TEAM

The team 'Molecular mechanisms of viral RNA translation' studies the influence of viral RNA structure on its translation by the cellular machinery. More specifically, the main research theme of the group is the translation of HIV genomic RNA and its regulation. It includes the study of the action of various proteins like helicases and methylases on the viral RNA structure, as well as the mechanism of translation initiation on HIV genomic RNA and the characterisation and faith of the peptidal products. The team is also involved in various collaborations to study the role of RNA structure on viral RNA translation in other models. In parallel, the team is also developing tools and methods for RNA secondary and tertiary structure prediction, integrating experimental and analytical data.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The first (and only) recommendation was about grants coordination and funding of the research outside the HIV field. The recommendation was fully taken into account: over the evaluated period the team obtained eleven grants, six of them as coordinator. The team was able to hire two postdoctoral students and two research engineers (with PhD); furthermore, only one of the grants was directly related to the HIV field, allowing sufficient funding for the other themes

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	**7**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	2
Sous-total personnels non permanents en activité	**2**
Total personnels	**9**

EVALUATION

Overall assessment of the team

Created in 2009, the team is a key player in the viral RNA structure/function field, thanks to its unique multidisciplinary approach, internationally renowned. The team has made extremely important contributions in the understanding of HIV genomic RNA biology, and was also able to set up one of the best pipeline for RNA structure prediction. These outstanding achievements still need to be confirmed by the acquisition of a European grant and by publishing in journals with a very broad audience and high visibility.

Strengths and possibilities linked to the context

To study the structure and function of viral RNA, the team set up, through recruitment and collaborations, a very exciting and convincing multidisciplinary approach, combining protein biochemistry, RNA molecular biology, cellular biology, lab automation, bioinformatics, computational physics and chemistry. The 'viral RNA structure/function' field is becoming more and more a 'hot' topic with obvious health and therapeutics implications; the team has all the cards to become a key player in this field at the local, national and international level.
The team managed to get eleven grants (6 as project leaders) and to secure more than 1.5 million euros to fund all their projects until the end of 2025. On top of that, more than 30 million CPU hours were obtained (~ 500,000 euros) for the MD simulation. And over the evaluated period, five PhD fellowships were awarded from the ministry of research.
The mentoring effort within the lab is a great asset as well and a big factor of attractiveness; five PhD students, three postdoctoral students and 25 undergraduates were trained during the evaluated period. All PhD students defended their thesis in less than four years with several publications as first – and co-author. All students and postdoctoral students were supported for the development of their career.
The local, national and international visibility of the team is outstanding in the field of RNA biology; the team set up several instrumental collaborations in France, Europe and in South America (LIA). Several senior team members have editorial responsibilities and organised conferences. Researchers and young scientists presented their work at national and international conferences (one PhD student award). Team members were invited to present their findings in France and abroad.
The team developed an internationally renowned and unique expertise in modelling RNA structure and they made this technology available to third parties as a collaboration or as a service. A technology transfer protocol is currently under discussion with Sanofi.

Weaknesses and risks linked to the context

Despite a significant number of national grants, no European funding was obtained during the evaluated period; the amount of money involved in these European grants (significantly higher than the national grants) could be the key to tackle the new challenges of the ever-growing RNA biology field, in terms of therapeutic targeting, RNA vectorisation, etc.
As a consequence of the latter point (or maybe as a reason), the team is lacking publications in very high visibility journals: although this lack is absolutely not representative of the outstanding quality of the work of the team, this reviewing committee has the feeling that the team has all what it needs to publish in such journals. Such publications would, of course, confirm and improve the international visibility of the team, secure more important funding and attract high-quality profiles for postdoctoral students and permanent positions.

Analysis of the team's trajectory

The team aims to continue its effort to develop multidisciplinary approaches to understand the structure, function and dynamics of RNA in various contexts. In order to expand its scopes, the team will expand its field of research from purely in vitro studies to *in cellulo* approaches. For this purpose, the team has already set up a cell culture activity within the group (baculovirus system for protein production, *in cellulo* RNA modification, viral infection models…) and also a collaboration with the group of Dr Marcelin about HIV and coronavirus with diagnostic and therapeutic perspectives. This more complete approaches of viral RNA biology will enable the team to apply for new types of grants (PEPR - Emerging Infectious Disease) and aim for journals with a wider audience and a better visibility.
In terms of scientific objectives, the team will develop three axes, all of them with clear potential applications in terms of innovative therapeutic targets, conception and production of mRNA vaccine:

- The study of cellular and viral proteins involved in RNA modifications.
- The understanding of RNA structure on viral RNA translation.
- The development of innovative and integrative methods to study RNA structure and interactions with small molecules.

These objectives are extremely ambitious and exciting as they fit perfectly with the scopes of the unit.

RECOMMENDATIONS TO THE TEAM

The team is on excellent tracks and the committee recommends to the team to continue their efforts to improve the visibility and attractiveness of the group.
The team should really put some efforts in obtaining European funding, maybe with the help of some dedicated service within the CNRS.
The committee also encourages the team to keep working with industrial partners: technology transfer, consulting, etc.

Regarding the small molecules and therapeutic target projects, the committee recommends to also rely on the expertise within the laboratory through collaborations with other teams of the unit: grant applications, students' co-supervision…

Team 4: Structural and functional studies of new therapeutic targets by NMR

Name of the supervisor: Mr. Serge Bouaziz

THEMES OF THE TEAM

The team has two major research axes on the identification and structural study of first antiviral targets and second antibacterial targets. The first axis is mainly focused on HIV but Sars-CoV2 was also introduced in 2020. The second axis concerns the development of new broad-spectrum antibiotics by targeting trans-translation processes and the characterisation of toxin peptides from *S. aureus*.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Collaborations with Citcom team 6 helped in obtaining a new funding. The number of PhD students was increased. No further contacts with the SATT or contacts with the industrial sector was developed.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	**5**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	0
Sous-total personnels non permanents en activité	**0**
Total personnels	**5**

EVALUATION

Overall assessment of the team

The scientific production of the team was very good considering its size. Low funding is a point of concern considering the burden of NMR spectrometer infrastructure. The currently presented number of research lines is worrying considering the size of the team and harmed its attractiveness. The arrival of a new PI with his own expertise and scientific objectives will be a challenge but also an opportunity to improve attractiveness and visibility that could be brought by a more coherent team project.

Strengths and possibilities linked to the context

The team has produced 24 publications during the reference period, nine as the first author and seven as the last author, in very well-reputed journals such as Nucleic Acids Research, European Journal of Medicinal Chemistry or Protein Science. They contributed several works on HIV virion genesis and maturation.

Four PhD students have joined the team including three funded by the Chinese Scholarship Council during this term. Three thesis were successfully defended and related publications were published as first authors.
One project was funded by idex, together with team six and some additional fund was obtained by providing NMR service measurements for other academic teams in France.
The team will benefit from funding for the installation of a helium recycling system and has coordinated a global effort on the Paris Cité campus to install such system at seven locations.
The team contributes to the national DyNAVir network and has organised locally two workshops in this framework.

Weaknesses and risks linked to the context

All PhD students were under the same supervisor.
Maintaining the NMR infrastructure is a heavy financial burden given the size of the team that should be alleviated by the Helium Recycling project.
The level of funding is low.
Too many and diverse research lines are followed by a team of limited human and financial resources.
No contact has been developed with the non-academic world, despite the opportunities provided by the NMR infrastructure in drug discovery process.

Analysis of the team's trajectory

The team focus is switching from HIV to Coronaviridae, and the skills acquired in virology through HIV will be a bonus to tackle this new target in a currently highly competitive field. Although the team has gradually recentred its activity on antiviral themes, many different projects and aspects are still ongoing. Contrary to previous recommendations, brand new and unrelated projects will be implemented in the team.

RECOMMENDATIONS TO THE TEAM

The collaborations inside the unit with chemists should be pursued and strengthened, notably in this Coronaviridae project as intended. The arrival of a new external PI for the team should be considered by team members as an opportunity to better focus the team project on a reasonable number of funded subjects and increase its attractiveness. In-cell NMR projects that will be implemented in the team might be a strong new force for the team to achieve these goals. These new projects are ambitious and will require the presence of dedicated technical staff.

Team 5: Analytical chemistry and experimental toxicology

Name of the supervisor: Mr. Olivier Laprévote

THEMES OF THE TEAM

The team main areas of expertise are chemistry (analytical chemistry, in particular mass spectrometry techniques, total synthesis, and natural products chemistry, all of which have synergies with chemoinformatics) and toxicology (cellular toxicology and metabolomic markers). The team has two technical platforms to support its research and development activities. The three main themes are 1) lipidomic aspects, in connection with toxicology 2) Neurodegenerative model for cell toxicology and identification of biomarkers and 3) Natural product chemistry, metabolomics assisted by computational chemistry.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Previous recommendations on scientific production and activities
The current scientific objectives and strategy are likely to produce even more outstanding achievements and should be pursued. The team could further enhance its international visibility by recruiting postdoctoral fellows from abroad. Although funding for doctorates is steady and high, sources of funding could be diversified to include more academic studentships. The transfer of technology and standardisation activities should be pursued and expanded. The valorisation through patents should be strongly considered if not already envisaged.

During this five-year period, the team focused primarily on cross-fertilising the different themes and valorising its results, in particular through the hPlacentox. Given the team excellent production and the good synergy between its themes and members, it has the capacity to further raise its international visibility. Looking for new sources of funding could provide the means to recruit foreign postdoctoral fellows who will enrich the team expertise.

Previous recommendations on the team's organisation and life

The merging of the two units could be a good opportunity for the team to create new interactions with other teams, particularly with future team 7. The scientific animation and communication should be improved in the future. Some seminars and groups meetings should be organised in collaboration with other teams. The team could benefit from further interactions with other teams.
The small size of the team has been cited as a reason for the weak scientific animation, particularly in terms of group meetings. Even if they are held less frequently, we recommend that they should be organised formally and regularly (rather than occasional or lunchroom meetings), with all members, as they are beneficial for the exchange of ideas and group cohesion. The suggestion to organise occasional meetings with other teams remains relevant to increase inter-team collaboration, even if strong collaborations are foreseen in the next contract, notably with team 7 following a recent recruitment.

Previous recommendations on scientific strategy and projects
The current scientific objectives and strategy are likely to produce outstanding achievements and should be pursued. Transfer of technology and standardisation activities should be pursued and expanded.

These comments have been considered and will be pursued in the next five-year contract.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	4
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	**10**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	4
Sous-total personnels non permanents en activité	**6**
Total personnels	**16**

EVALUATION

Overall assessment of the team

The team' production is good to excellent, and its complementary expertise ranges from analytical chemistry by mass spectrometry, natural product chemistry and total synthesis, to topics related to cellular toxicity. The team has a good reputation in its fields of expertise, but could eventually gain in visibility by publishing more in generalist journals.

Strengths and possibilities linked to the context

The axes developed are both promising in their respective fields, but also open to interaction with other axes, notably through chemoinformatics, or the complementarity between metabolomic analysis of biomarkers and cellular toxicity. Each axis is led by a PI who is recognised in his field. Thanks to their strong investment, the PIs in charge of these areas have a very good to excellent scientific production, and contribute to the success of local and national calls for projects. The team thematic areas are a source of scientific innovation: new synthesis and analysis methodologies, the use of DFT as a synthesis strategy, chemo- and bioinformatics for chemical and metabolomic analysis, development and valorisation of new cell-based tests, with the creation of a new platform within the team. The team leader is internationally recognised for his many responsibilities and conferences. The two platforms (Mass spectroscopy with strong lipidomic know-how and the new Cellular toxicology platform) are useful elements, both for the team research and for the link created with the needs of the hospital and the economic sector. These platforms also facilitate the flow of financial incomes and collaborations. This link with the non-academic sector is reflected in Cifre PhDs (4) focused on each main theme. A close relationship has been established with a company to conduct research with dedicated staff within the team. The team is highly involved in training students for research (7 PhDs defended and 7 PhDs ongoing).

Weaknesses and risks linked to the context

Given the team scientific production and the technical environment, the team has not initiated any response to international calls for project funding. Increasing national and international visibility also requires all team members to be present at international conferences to give lectures and oral presentations. This task falls mainly to the team leader. The quality of the building and the resulting working conditions are a major obstacle to the attractiveness and the well-being of the staff. The team should also make efforts to reach out to the general public in terms of communication and knowledge transfer. One risk for the team interconnectivity is the

departure in 2021 of a MCU with chemoinformatics expertise. He is also a key contributor to the team, with numerous collaborations and papers to his credit. As the 'Chair de Professeur Junior' (CPJ) operation to recruit a new full professor was unsuccessful, the question of renewing the team leader in future remains unclear.

Analysis of the team's trajectory

The main areas of research will continue. A major focus will be on lipidomics, i.e. the study of lipid variation under the influence of the environment (pollutant/contaminant/drug) and xenometabolome involved in poisoning of patient. Metabolomic research on highly polar or highly volatile metabolites will require the development of adapted techniques. Collaboration on plant and human metabolomics with Team 7 is envisaged thanks to the arrival of a MCU. This axis represents a high-potential trajectory for understanding the relationships between living organisms and their environment. The hPlacentox assay will continue to be developed, with the help of the partner company. The ambition is to achieve European recognition as a reference in this field. To achieve this, new tests will be developed (ovarian, 3D placenta). New collaborations are envisioned with different Citcom teams and national partners to perform cell toxicity assays. In the field of synthetic chemistry, ambitious total synthesis projects and new synthesis methodologies will be launched, in particular for natural products with antibiotic and anti-cancer activities. The synthetic challenge is remarkable. Regarding the two platforms, the creation of a mass spectrometry platform for the hospital's ophthalmology service is underway and will ensure a stronger link with the hospital. During the presentation of the trajectory by the team leader, the future of the cellular toxicology platform in the team remains unclear as to who will be involved in the next period.

RECOMMENDATIONS TO THE TEAM

The team has an excellent scientific production and state-of-the-art technical infrastructure to carry out ambitious projects. Under these conditions, it would be appropriate to seek European and international funding to increase visibility. The organisation of formal group meetings would be welcome to cross-fertilise new ideas, and occasionally organise exchanges with other groups that could lead to new inter-team collaborations. The team has the ability to target more generalist journals as corresponding author to gain greater visibility. Publications in fast-track journals should be taken with caution. The team should consider finding a way to reconsolidate its expertise in computation chemistry and clarify the situation for the cell toxicology theme.

Team 6: Medicinal chemistry and translational research

Name of the supervisor: Mr. Michel Vidal and Ms. Maria Miteva

THEMES OF THE TEAM

The team is specialised in medicinal chemistry, historically mainly in the field of cancer. The therapeutic areas expanded during the past period to inflammation and infectious diseases. The expertise goes from molecular modelling, organic chemistry (heterocyclic and peptidic), medicinal chemistry and in vitro evaluation. Thanks to the hospital activities, the projects also include the study of anticancer drug mechanisms and biomarkers, therapeutic drugs monitoring.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

There is a noticeable lack of publications in very high impact journals:
More than 100 articles have been published, with 2 in highly visible journals

Collaboration with industry in a framework of public-private partnership could be enhanced. Public outreach to explain medicinal chemistry research to the public is desirable.
A new member of the team is the founder of a start-up company (IPCure). A collaboration was developed with Allspim company. Communication to the public was developed.

The number of PhD students is moderate. The number of habilitated scientists (3) could also be increased.
The number of PhD students increased (+4). Three new habilitated scientists joined the team, and one MCU obtained the HDR in 2017.

This group has faced important turnover of researchers, which should be controlled. The team is dispersed on 4 different sites of the faculty.
Three scientists have joined the team, and no turnover has been noted. The lab space seems to remain a weakness.

Competition in the field of drug discovery is extremely strong and the team somehow misses a clear valorisation strategy as the first step in all its projects in order to remain competitive. A validation step towards animal models is missing, which would enable proof of concept necessary for the valorisation of new pharmacological agents.
Valorisation strategy was clearly improved with patents and the creation of a start-up. For in vivo experiments, the team started collaboration on new projects.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	3
Maîtres de conférences et assimilés	6
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	**15**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	1
Doctorants	10
Sous-total personnels non permanents en activité	**12**
Total personnels	**27**

EVALUATION

Overall assessment of the team

The team is recognised for its expertise in drug design, medicinal chemistry and translational research. Its scientific output is excellent despite important teaching activities and collective responsibilities of its members. The team's attractiveness is excellent, as demonstrated by the number of PhD students supervised and international collaborations. The level of interaction with the socio-economic world is excellent, as are the team's actions towards civil society. The trajectory presented is in adequation with the expertise development of methodologies and drug design and synthesis, even if presented separately.

Strengths and possibilities linked to the context

The team has a large panel of expertise: from molecular modelling to chemistry and hospital applications. This expertise is highlighted in the multiple research projects.
The level of the scientific production is very good, with articles in well-regarded journals of medicinal chemistry (e.g. J. Med. Chem., ACS Chem Biol., Sci. Rep., Drug Discov Today), communications in meetings by young researchers or as invited lecturers, including at the international level (e.g. 'AI for drug discovery', Lisbon - 2018).

The team has a very good valorisation strategy, with the creation of one start up (initiated by a recent member of the team), four patents and one protected software (drugME).

The team succeeded in grants' applications: five ANR projects (global amount: 639 kE), one idex grant and others, for a total amount of 1,294 ME

The members of the team have an important involvement in research organisation: meeting organisation, board of editors, research and grant evaluation (ANR, Hcéres, international projects…), SAB of scientific societies, Académie,…

The team has numerous national and international collaborations

Weaknesses and risks linked to the context

The number of projects (several/researcher) is huge and the rationale for the choice of the projects is not clear. No focus seems to be put on a particular family of target or compounds or therapeutic axis.

Although the drug discovery process is a continuous and collaborative aim, the team looks like the addition of two independent groups, with only the caspase project gathering chemists and AI researchers. At that time, there is no paper gathering the two groups. In addition, the collaborations with the other teams of the unit are underdeveloped, with only two projects under evaluation and six papers/111 with members of other teams.

Though the team succeeded in getting national grants, there is no international ones

The number of post doctorates is limited and should be increased thanks to significative grants.

Analysis of the team's trajectory

The strategy of the team will remain the same as it was, with new thematic (infection and inflammation, in addition to oncology). The two axes in methodology will remain separated but the members of the two groups will participate in common projects.

RECOMMENDATIONS TO THE TEAM

The team has a large panel of expertise, from molecular modelling to chemistry and in vitro evaluation. The team should benefit from this expertise to develop the projects together and increase the impact.
The number of research projects was found very large. For some projects, the team is at the origin, for other the team answers external request. The committee advises the team to focus on a smaller number of projects and rationalise them (same type of targets or approaches). Challenging projects could be prioritised.
With such a team, the international visibility should be increased. The committee encourages the team to capitalise on existing collaborations to enhance international recognition through increased participation in international congresses and European consortia and applications to international grants.

Team 7: Natural products, analyses and syntheses

Name of the supervisor: Mr. Philippe Belmont

THEMES OF THE TEAM

The scientific activities of the PNAS team (team 7) focus on natural product chemistry in all its scientific aspects (extraction, structure elucidation, extract analysis, semi-synthesis, medicinal chemistry), as well as on the development of various synthesis methodologies (organic, organometallic, photocatalysis) and total synthesis. The team aims to exploit the compounds obtained by purification from natural resources or by organic synthesis, mainly for applications in the field of human health. The team also conducts original research on the toxicological aspects of certain natural products and falsified drugs. Finally, the PNAS team has defined green and biobased chemistry as a federative axis.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The new team leader has instilled a dynamic which has enabled to answer most of the recommendations from the previous evaluation. The scientific signature of this research team, which has a strong background in NP chemistry, was very clearly defined during the committee's visit.
Interactions have been strengthened regarding scientific production and activities, focusing on 3 highly interconnected scientific thematic axes. Participation in international conferences is limited and could be increased.
Regarding team life, regular meetings are organised, and interactions with biologists and the hospital sector for clinical development are numerous. The recent recruitment of a MCU has also enabled the integration of the 'biotransformation' activity. Finally, two colleagues working in molecular genetics will soon join the team.
Recruitment of young CRs CNRS is difficult, given the limited number of positions open to competition and the poor quality of the infrastructure.
Regarding scientific strategy and projects, it is strongly recommended to step up interactions with academic and private biology and pharmacology teams to streamline research into structures with high therapeutic potential. Interactions with the industry could be further improved. Although the link of the methodology in organic synthesis with the unit's other themes was unclear from the DAE, the presentation cleared up doubts and brought all the PNAS team's themes into perfect coherence.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	5
Maîtres de conférences et assimilés	14
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	**25**
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	10
Sous-total personnels non permanents en activité	**12**
Total personnels	**37**

EVALUATION

Overall assessment of the team

The team is recognised for its expertise in natural product chemistry. Its scientific output is excellent, although many of its members have important teaching activities and collective responsibilities.
The team's attractiveness is outstanding, as demonstrated by the number of supervised PhD students and international collaborations. The level of interaction with the socio-economic world is excellent, as are the team's actions towards civil society. The trajectory presented is likely to position in few years the PNAS team as a major pole of natural product chemistry at national and international levels.

Strengths and possibilities linked to the context

Team members have specific and varied skills in natural product chemistry (isolation of original bioactive compounds and structure determination, toxicology aspects, CPC, etc.), recognised mainly at the national level but also internationally in some cases.
The team has a dynamic approach to proposal submissions and funding raising, mainly at the local and national levels. Interactions with industry have resulted in one Cifre thesis.
Thirty PhD students were funded during this contract period. This financial autonomy enables the team to support 'risky' research themes such as medicinal chemistry of natural substances.
The team's scientific output is excellent, with 153 articles or book chapters published during the period, representing around 2.1 articles/ETP/year. Publishing in a broad audience and high visibility journal is not always easy for specific themes.
Of special relevance is a network of international collaborations (Argentina, Brazil, Italy). There are numerous collaborations with teams of biologists and/or hospitals, which is an asset in terms of translational research.
Team members are heavily involved in collective tasks (committee of the Faculty of Pharmacy, director of a multidisciplinary Doctoral School, etc.) and national expert missions (Académie Nationale de Pharmacie, EDQM, SCT, etc.).
The team has recently (2022) acquired a biotransformation laboratory (security level 1 – L1), which is consistent with the team's scientific project.
Structuring part of the equipment into a platform (CAP-42) has enabled the team to rationalise its maintenance and use.
Involvement in aspects of science with and for the society is excellent. In this respect, the work started to promote the Tillequin Museum is essential, given the inestimable value of this unique collection.

Weaknesses and risks linked to the context

Reducing the number of themes from 4 to 3 will increase transversality within the team. The links between the various aspects of natural product chemistry, particularly those about organic synthesis methodology, were clearly set out during the committee's visit.
Links and collaborations with other teams in the research unit were not clearly mentioned in the DAE, but were presented during the committee's visit. Nevertheless, the added value of belonging to a unit such as Citcom is not clearly apparent.
Despite a strong network of international collaborations, indicators of international recognition (invited conferences, international and European projects, hosting of international colleagues, etc.) could be further improved.
The team does not appear to be involved in PEPR.
The team does not appear to have developed specific skills in modern tools concerning phytochemistry, particularly in the fields of chemoinformatics and separative sciences. This point needs to be improved.
The lack of a detailed scientific section makes understanding the strategy for sourcing natural substances and identifying biological targets difficult.
The quality of the infrastructure is a major drawback in terms of attractiveness, and the risk of key skills disappearing (age pyramid, for example) does not help us to have a precise vision of human resource evolution.
The CAP-42 platform is highlighted in the DAE. However, this platform does not benefit from any special arrangements, labels or certifications. Nevertheless, it appears to be a very useful support for methodological research.
To the detriment of research, some team members are heavily involved in expertise work and collective tasks.

Analysis of the team's trajectory

The PNAS team's scientific project aligns with the trajectory defined during the previous contract, and several funding opportunities have been obtained in key areas that will continue in the coming years. The team's well-defined strategy will enable it to position itself internationally. The federating keywords will be: omics and biotechnology, development of analytical methods and methodology in photoredox catalysis, and photochemistry.
Green chemistry is one of the strengths of the research project, both in phytochemistry and in the development of separative or synthetic processes. Moreover, the coming years should see an increase in biotransformation activities.
In the phytochemistry, semi-synthesis and green processes research axis, an interesting project on NADES will be developed in collaboration with Team 5. The potential of CPC for industrial applications or purification of compounds derived from organic synthesis will be explored, although the associated research questions will not be specified. Semi-synthesis of compounds of interest, such as isoprostanes, will be pursued to develop anti-inflammatory, neuroprotective and antiarrhythmic active substances.
Within the analytical phytochemistry axis, original work on adulterated drugs and the toxicity of natural substances will be continued, focusing on furan toxins. In addition, using micro-organisms to carry out biotransformations will be an essential theme for the PNAS team.
The methodology, total synthesis and green chemistry axes will see all the team's activities tinged with green chemistry. Work has been carried out to improve the interface with the rest of the team, with a clear link to natural substances and therapeutic applications. The synthesis of original peptidomimetics for applications in antibiotic therapy is on the agenda. In addition, several projects have catalysis as a unifying theme, such as silver, nickel or visible light (photocatalysis/photochemistry).
Finally, the analytical study of samples preserved at the Musée F. Tillequin will support an ambitious project to study the traceability of ancient 'Cayenne incense' samples in collaboration with Ecole Polytechnique and ICSN.

RECOMMENDATIONS TO THE TEAM

First and foremost, the committee recommends that the team continue along the path it has embarked on, which aims to synergize all its skills around natural product chemistry while maintaining close links with the biology and hospital sectors. In addition, the efforts to promote the museum's collections are an excellent initiative. Research into the toxicological aspects of certain natural substances and the problem of counterfeit drugs is a specificity of the team that should be maintained and even developed.
The committee encourages the team to capitalise on existing international collaborations to strengthen international recognition through increased participation in international congresses and European consortia.
Methodological developments and the introduction of modern tools, particularly in phytochemistry, need to be intensified. The same applies to the role of green chemistry and biosourced chemistry. The committee recommends that fundamental research questions and the associated scientific obstacles be clearly identified and considered.
The desire to develop facilities dedicated to activity in the field of biotransformations is truly relevant. The project is ambitious and will require the presence of dedicated technical staff.
Lastly, the committee recommends that the team pursue its communication initiatives for a broad audience. Publications in fast-moving journals should be treated cautiously.

CONDUCT OF THE INTERVIEWS

Dates

Start: 29 janvier 2024 à 14 h

End : 30 janvier 2024 à 16 h

Interview conducted: on-site or online

INTERVIEW SCHEDULE

Monday, 29 January 2024
12:30 Lunch and meeting of the expert committee (closed hearing)
1:30 p.m. Presentation of the Hcéres evaluation to the unit (CS)
1:35 p.m. – 2:35 p.m. Presentation of the research unit by the Director + Plateforms (40' + 20'discussion)
2:35 p.m.-2:45 p.m. Break/debriefing committee
2:45 p.m. Team presentations (30 min – 15' talk +10' discussion +5' PI only)
2:45 p.m.-3:15 p.m. Team 1 – Molecular RNA machineries and human pathologies
3:15 p.m.-3:45 p.m. Team 2 – Signalling and membrane transport group
3:45 p.m.-4 p.m. Break/debriefing
4 p.m.-4:30 p.m. Team 3 – Molecular mechanisms of viral RNA translation
4:30 p.m.-5 p.m. Team 4 – Structural and functional studies of new therapeutic targets by NMR
5:10 p.m.-6 p.m. Visit of the laboratory premises (committee/DU)
Debriefing + Dinner (Committee + CS)

Tuesday, 30 January 2024
9:00 Team presentations
9:00-9:30 Team 5 – Analytical chemistry and experimental toxicology
9:30-10:00 Team 6 – Medicinal chemistry and translational research
10:00-10:30 Team 7 – Natural products, analyses and synthesis
10:30-10:45 Break
Interviews (closed sessions) – 10:45-12:30
10:45-11:15 Meeting w/Units' technical staff (no DU board)
11:30-12:00 Meeting w/PhD students and postdoctoral fellows
12:00-12:30 Meeting w/researchers and teachers (no team leaders)
12:30-1:30 p.m. Debriefing and Lunch
1:45 p.m.-2:15 p.m. Meeting w/supervising bodies (UPC, CNRS, Inserm) /
VP UPC Zoom link:
https://hceres-fr.zoom.us/j/91460153116?pwd=eXlQTzBwNEE0UEJiQkFqekFucDlVUT09
Meeting ID: 914 6015 3116, Passcode: 204,416
2
2:30 p.m. Meeting with the DU/Unit directory board
3 p.m.-4 p.m. Debriefing of the committee/Report writing

PARTICULAR POINT TO BE MENTIONED

N/A

GENERAL OBSERVATIONS OF THE SUPERVISORS

Université Paris Cité

Le Président

Paris, le 8 Avril 2024

HCERES
2 rue Albert Einstein
75013 Paris

Objet : Rapport d'évaluation de l'unité **DER-PUR250024164 - Citcom - Cibles thérapeutiques et conception de médicaments**.

Madame, Monsieur,

L'université Paris Cité (UPCité) a pris connaissance du rapport d'évaluation de l'unité Citcom - Cibles thérapeutiques et conception de médicaments. Ce rapport a été lu avec attention par la direction de l'unité (de la part de laquelle vous trouverez deux courriers joints), par le doyen de la Faculté de Santé d'UPCité, par la vice-présidente Recherche d'UPCité et par moi-même. L'ensemble des acteurs UPCité remercie le comité pour son travail d'évaluation.

Le doyen de la Faculté de Santé et moi même souhaitons souligner que l'UMR CiTCoM mène des travaux de recherche alliant la biologie et la chimie afin d'accélérer la conception de médicaments. Le dernier quinquennat aura permis l'intégration réussie (en terme de projets, succès aux appels à projets, publications) de deux unités de recherche, l'une plutôt orientée vers la biologie et l'autre vers la chimie. Le CiTCoM s'inscrit parfaitement aujourd'hui dans la politique scientifique de la Faculté de Santé et de l'université, et participe à la restructuration de la recherche sur le site de l'UFR de Pharmacie.

Nous vous remercions aussi pour vos alertes, orales et écrites, concernant l'état de conformité de certaines sorbonnes, et l'état du batiment. Nous allons veiller en priorité, avec le directeur de l'UFR de Pharmacie, à ce que la sécurité des étudiants soit scrupuleusement garantie en demandant à la direction de l'unité d'interdire formellement l'accès aux sorbonnes non-conformes. La dégradation du site historique de l'Observatoire, liée notamment à des infiltrations au niveau du toit et des ouvrants, fait partie des problématiques immobilières complexes auxquelles doit faire face notre établissement. Nous travaillons avec l'Établissement Public d'Aménagement Universitaire de la Région Ile-De-France (Epaurif) à la mise en œuvre des refections prévues dans le cadre des financements obtenus dans le cadre du plan Campus.

Je vous prie d'agréer, Madame, Monsieur, l'expression de ma considération distinguée.

Édouard Kaminski

Présidence

Référence
Pr/DGDRIVE/2023

Affaire suivie par
Christine Debydeal - DGDRIVE

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Pr Nicolas Leulliot
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URL: http://www.citcom.cnrs.com

Paris, 22 mars 2024

Objet : Observations de portée générale sur le rapport HCERES de l'Unité CiTCoM

Madame, Monsieur,

Nous remercions le comité pour le rapport d'évaluation de notre Unité, qui n'appelle pas de remarques particulières de notre part.

Bien cordialement,

Pr Nicolas Leulliot

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