

EVALUATION REPORT OF THE UNIT
ARN - Architecture et réactivité de l'ARN

UNDER THE SUPERVISION OF THE
FOLLOWING ESTABLISHMENTS AND
ORGANISMS:

Université de Strasbourg,
Centre national de la recherche scientifique –
CNRS
Ministère de la Culture et de la Communication
- Architecture

EVALUATION CAMPAIGN 2022-2023
GROUP C

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In the name of the expert committee¹ :

Antonin Morillon, Chairman of the committee

For the Hcéres² :

Thierry Coulhon, President

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

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

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

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

MEMBERS OF THE EXPERT COMMITTEE

Chairperson: Mr Antonin Morillon, CNRS, Paris

Mr Jean-Luc Battini, Inserm, Montpellier
Mr Frederic Boccard, CNRS, Gif-sur-Yvette

Experts:

Mr Christophe Bordi, Aix-Marseille Université AMU (representative of CNU)
Mr Alexei Grichine, université Grenoble Alpes — UGA (representative of the supporting personnel)
Mr Alexis Verger, CNRS, Villeneuve d'Ascq (representative of CoNRS)

HCÉRES REPRESENTATIVE

Ms Ina Attrée

CHARACTERISATION OF THE UNIT

- Name: Architecture and Reactivity of RNA/Architecture et Réactivité de l'ARN
- Acronym: ARN
- Label and number: UPR 9002
- Number of teams: 10
- Composition of the executive team: Dr Pascale Romby

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 ten teams share a central objective: deciphering the function of the RNAs molecules in the regulation of gene expression especially the role and the control of the translation machinery. The mechanistic dissections of the different classes of regulatory RNAs and their associated machineries from eukaryotic miRNAs, bacterial RNAs, tRNAs, or viral RNAs are studied in details in different models such as yeast, anopheles, mammals but also pathogens as viruses, bacteria and parasites. Thus the unit has the capacity to leverage understanding of biological phenomena from molecules to phenotype and exploits its basics research and methodological know-how for biotechnology.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The UPR 9002 was created in January 2005. It is one of the three CNRS units (UPR) constituting the Institute of Cellular and Molecular Biology (IBMC), organised as a CNRS Federation of Research Units (FRC 1589) within one building. The institute is located in the Strasbourg University campus in the city. The unit has strong links with the University of Strasbourg and other research institutes.

RESEARCH ENVIRONMENT OF THE UNIT

The Unit ARN is one of the three units of IBMC (Fédération de Recherche FR1587) hosting around 200 person total. The three research Units: — UPR 9002 — ARN « Architecture and Reactivity of RNA » (100 members, Dir. P. Romby) – UPR 9022 – M3I 'Insect models of Innate Immunity' (60 members, Dir. J.-L. Imler) – UPR 3572 – I2CT 'Immunology, immunopathology and therapeutic chemistry' (30 members, Dir. H. Dumortier). IBMC (created in 1974) is a multidisciplinary (biochemistry, molecular and cell biology, immunology, chemistry, and biophysics) research institute, studying gene expression in various organisms. The IBMC provides material support for research and the grouping of the three research Units to facilitate the interaction within different expertises.

The Unit ARN has been supported by Future Investments Program (PIA), for which they coordinated the Laboratory of Excellence NetRNA (2011–2021, P. Romby since 2016). This network, with fifteen teams (6 from ARN, 4 from M3i, and 5 teams from IBMP-UPR 2357), investigated the non-coding genome across kingdoms, providing advanced interdisciplinary research and training. The ARN Unit (team E13) has also been partner of the LabEx MitoCross (2012–2021, dir I. Tarassov GMGM-UMR 7156), investigating the crosstalks between the mitochondria/nucleus and cytoplasm. NetRNA has reinforced the IBMC proteomics and IBMP imaging platforms. Additional funds and engineer positions were obtained from IdEx (Unistra), the CNRS and the Region Grand Est. The Unit ARN was also part of the EquipEx I2MC infrastructure (2011–2021, dir by J.-L. Imler). NetRNA has also promoted collaborations with the other LabEx consortia HepSYS, MitoCross, INRT (IGBMC), and Medalis. Three different labex (INRT, MitoCross and NetRNA) cofounded the Graduate School IMCBio (2018– 2028, PIA3 directed by B. Seraphin and N. Matt). Five ARN teams are part of two ITIs (InnoVec and IMCBio+). Innovec together with nine research Units (ESBS, iCube, Faculté de pharmacie et médecine, IBMC) promotes solutions for the vectorisation of active biomolecules (bacteria resistance and aggressive cancers). The IMCBio+ institute (dir P. Romby) comprises the Graduate School IMCBio and four LabExes (HepSYS, INRT, MitoCross, NetRNA) to federate five institutes (IGBMC, IBMC, IBMP, GMGM, IVH) to decipher the complexity of living organisms and to transfer fundamental knowledge to application.

The ARN Unit (P. Romby) coordinates EpiARN 'Ribonucleoprotein particles and Epitranscriptomics' consortium (Region Grand Est funding 2017–2023). This funding provides support for equipment and salaries in order to develop innovative methodologies to map RNA modifications and to analyse the structure and dynamics of RNA machineries.

Finally, the ARN Unit is partner of the CPER ImaProGen (Contrat de plan Etat-Région 2021-2027) that provides support for platforms and infrastructures.

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

Permanent personnel in active employment	
Professors and associate professors	2
Lecturer and associate lecturer	6
Senior scientist (Research Director, DR) and associate	15
Scientist (Research Fellow, CR) and associate	8
Other scientists (EPIC researchers and other organisms, foundations or private companies)	0
Research supporting personnel (PAR)	23
Subtotal permanent personnel in active employment	54
Non-permanent teacher-researchers, researchers and associates	6
Non-permanent research supporting personnel (PAR)	7
Post-docs	6
PhD Students	31
Subtotal non-permanent personnel	50
Total	104

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

Employer	EC	C	PAR
CNRS	0	21	21
Université de Strasbourg	8	0	2
Inserm	0	2	0
Total	8	23	23

UNIT BUDGET

Recurrent budget excluding wage bill allocated by parent institutions (total over 6 years)	2189.0
Own resources obtained from regional calls for projects (total over 6 years of sums obtained from AAP idex, i-site, CPER, territorial authorities, etc.)	846.0
Own resources obtained from national calls for projects (total over 6 years of sums obtained on AAP ONR, PIA, ANR, FRM, INCa, etc.)	6111.0
Own resources obtained from international call for projects (total over 6 years of sums obtained)	1761.0
Own resources issued from the valorisation, transfer and industrial collaboration (total over 6 years of sums obtained through contracts, patents, service activities, services, etc.)	571.0
Total in k €	11,478.0

GLOBAL ASSESSMENT

The RNA unit aims to decipher the function of RNA molecules during the regulation of gene expression, in particular their role in the control of the translation machinery. The different classes of regulatory RNAs and their associated machineries, miRNAs, bacterial RNAs, tRNAs or viral RNAs, are studied in detail in different models, such as yeasts, Anopheles, mammals but also pathogens such as viruses, bacteria and parasites.

The scientific production during the period was excellent with important contributions in several fields of RNA, including in human diseases, illustrated by an excellent level of publication. The unit has maintained a leading project based on its historical expertise on RNA biology and its ability to implement cutting-edge technologies. The scientific production is of a very high level and of excellent quality, with an outstanding publication rate given the unit's size with a total of 278 publications (including 9 BioRxiv manuscripts, 29 involving two or three teams from the unit and 31 reviews; 71% as lead authors). The total number of citations for the period is 6443, including those for generalist journals (2 Science, 4 PNAS, 7 Nature Comm, 9 Scientific Reports, 3 EMBO J, 1 EMBO Rep, 2 Cell Rep, 1 Mol Cell, 2 Elife). Most of the teams published at very high level. Only three doctoral students out of 46 defended theses had not published their work when the thesis report was written.

The visibility of the unit is outstanding at the local and national levels with specificities and strong relations with the University of Strasbourg through the ITIs and the LabEx. The unit is also a leader of the laboratory network in the Grand Est territory for the project on epitranscriptomics. This allows the unit to be closely involved in teaching and training students at all levels. The unit has excellent international visibility (hundreds of invitations to international events). In return, the attractiveness is excellent not only for recruiting young scientists, from PhD level to team leader (45 PhD recruitments and 3 team leaders). The expected turnover and departures of the recent years nevertheless will lead to more regular recruitments of new teams. The attractiveness is also remarkable for attracting local, national and international funding (1 private contract, 3 ERC, 2 Marie Skłodowska-Curie, 1 ERA-Eurostars-2, 2 Cost, 1 international research project, 4 bilateral financial supports, 2 labex, 1 equipex, 2 ITI, 2 doctoral schools and finally 30 ANR with 17 in leading position, 4 FRM, 7 sidaction, 1 AFM, 1 league and 1 CPER). Annually, the Unit's overall budget is approximately €2 million (excluding salaries for permanent positions), 85% of which comes from external funding (excluding CNRS and the university).

The Unit promotes excellent interactions towards the non-academic (hospitals, companies), and initiates products towards the socio-economic world (13 patents, 2 declarations of invention, 4 pre-maturation projects, creation of the start-up MicroOmix and the renewal of the Labcom DiagnOxi). In recent years, the technology transfer has been facilitated by the internal training of Unit members, including PhD students with the help of IMCBio and Satt Conectus. Several teams have collaborative projects with hospitals (e.g. team E05-Institut Pasteur; team E09-Lyon hospital; team E04-guest member of the American Charity Cure for Congenital Muscular Dystrophy and contact with families). Several partnerships with companies have been set up (E01-Sanofi-Cifre; Eurostars2; E02-NovAliX; E10-Novaptech).

Finally, the unit has been involved in regular promotions for biology and infectious diseases studies for the benefit of the society through academic communications, open science and the dissemination of information to the general public (Fête de la Science, design of videos, photos and posters, organisation of events with schools, crystallization competitions, RNA video sketches, 'my thesis in 180 sec'). Several staff members have been active during the Covid pandemic in explaining RNA research and the importance of basic science that led to the concept of RNA vaccines (TV, articles, and radio interviews).

DETAILED EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Scientific quality and outputs

'The focus of the unit on a central research object and the diverse methodological skills in the various teams may favour the emergence of more transverse projects. This would probably be beneficial to the unit'

The ARN unit perfectly responded during the last term to these recommendations by recruiting high-level engineers to reinforce the teams which develop innovative methods (ITC microcalorimetry analysis; bioinformatics for specific analysis of NGS data; biophysical methods, development of RNA-RNA, and RNA-protein interactions; bioinformatics and deep learning applied to microfluidics. The Unit has provided initiative for transversal projects that resulted in collaborations involving at least two different teams and led to 30 publications.

Academic reputation:

The emergence of new research themes and methodologies, such as microfluidics and cryo-EM, should lead the unit to enlarge its international audience and to construct new networks of collaboration.

Despite having considerably increased further its visibility within Strasbourg and in France, the unit did not really improve its international visibility through European or international networks which remained an aspect of improvement within the coming years.

Unit interaction with the social, economic and cultural environment

It may be beneficial to perform a thorough analysis of partnerships and to negotiate formal contracts in which the benefit for the unit is clear.

The Unit tried to clarify this aspect by initiating regular discussions with the Satt Conectus and the Valorization office of the CNRS to help the unit members with the detection of inventions, technology transfers, and proofs of concept and maturation of inventions. Within the LabCom, the Unit/CNRS and the company share equal governance. A correspondent in charge of valorisation and partnerships assists the director of the Unit allowing the relations with companies to be clarified, leaving though some more to improve.

B – EVALUATION AREAS

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

Assessment on the unit's resources

The Unit has an outstanding organisation of the resources with a common budget (60% of the CNRS funding, 100% of the university funding and 25% of the external contracts). A lot of effort has been put into central common services and mutualization of equipment, consumables and human resources. The outstanding capacity to attract external grants (such as IdEx, LabEx, ANR, or ERC) brings in more than 1.9 M€ per year. Key engineers have been recruited (3) and researchers brought new expertise to the Unit (3 CRCN CNRS, 2 MCU and 1 DR2 Inserm) participating in the expansion of the know-how.

Assessment on the scientific objectives of the unit

The ARN Unit is very well focused and coherent with ten teams developing distinct facets of RNA biology focused on infectious disease, involving several model systems (from yeast, anopheles, mammals to pathogens as viruses, bacteria and parasites). During the last period, the research interests have moved towards a more integrative biology (from structural biology to genetic/omic/microfluidics approaches), providing an excellent stimulating research environment, with real synergies between the teams (as marked by more than 30 collaborative publications within the unit teams).

Assessment on the functioning of the unit

The human resources management of the unit is excellent with great care in gender equality and non-discriminatory (website, seminars and exhibitions on gender disparity, surveys...). The unit has an excellent organisation to monitor working conditions and protection of the scientific assets – 2 Safety Officers, fire safety team members, a 'Document Unique' and a Covid19 activity plan, a computer Charter –. The Unit has a very good risk prevention for environmental protection and the pursuit of sustainable development goals (1 person for communication and a green committee at the IBMC level).

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

Strengths and possibilities linked to the context

The Unit is organised around central common services (secretarial and financial expertise). Many goods, consumables, chemicals, and small equipment are mutualised in the central budget as well as the scientific animation, remodeling of the laboratories and offices, the retreat of the Unit and most of the heavy equipment and maintenance costs. The central budget is fed by 60% of the core funding from the CNRS, 100% of the Unistra funds and by 25% (excluding salaries) of the contracts granted to the teams. The distribution of the central budget and the allocation of the remaining 40% of the CNRS core funding to the different teams are discussed during specific meetings. The main support comes from the CNRS with 300 k€ yearly and about 49 k€ from the University of Strasbourg, on average.

The external grants are highly diverse – e.g. Investissement d'avenir (IdEx Unistra, LabEx), ANR, ANRS, Bilateral exchange programs, European networks, ERC – and bring in more than 1.9 M€ on average per year representing more than 85% of the total budget. The ANR (30 grants) has been one of the main sources for external funding over the period – seventeen as coordinator and two international ANR-DFG grants. In addition, the Unit is a partner and coordinates two labExes, and more recently two ITI (InnoVec and IMCBio+). 1 ERC Consolidator Grant in 2015, and starting ERC grant in 2017. Three Marie Curie contracts have been obtained, and bilateral collaborations were funded (IRP and bilateral grants with several countries). Contribution of funds coming from partnerships with companies (LabCom with Adisseo, E04; European contract with Dynamic Biosensors, E01; Sanofi, E01), from the Satt Conectus (pre-maturation and maturation contracts, E01, E07, E10), and from the Plan de Relance (Novalix, E02; Novaptech, E10). Finally, other funds are coming from the region Grand Est, and several associations supporting research linked to human pathologies (FRM, ARC, Ligue contre le Cancer, AFM...). Annually, the overall budget of the Unit is around two M€ (excl salaries for the permanent positions).

During these last six years, key engineer CNRS positions have been recruited – IR2 CNRS for the INSTRUCT-Eric advanced microcalorimetry platform, IR2 CNRS developed strategies of microfluidic devices, IECN CNRS developing novel methods to map RNA structure, IECN CNRS as the bioinformatician to analyse and develop tools for NGS data analysis. Besides, several researchers brought new expertise to the Unit (CRCN CNRS, NMR, team E01, CRCN Inserm, cryoEM, team E01, CRCN CNRS, RNA interactome, team E09, MCU, RNA regulation in bacteria, team E10, MCU, genetic screens, team E08, DR2 Inserm, *Shigella* infection).

This was also accompanied by additional CNRS funds allowing the acquisition of the switchSENSE technology (2016), a Biocomp gradient fractionator (2017), the vitrobot (2017), a robot for crystallization assays (in 2018), and a multifunctional microbeta apparatus (2020).

Weaknesses and risks linked to the context

No major weakness, but while the excellent structuration and cohesion of the different Labex and ITI for the unit and platforms, it might cause some dissociation effects for teams which do not belong to such organisations. For instance, it had some impacts on the recruitment of PhD students through the graduate school ICMBIO+++. In addition, there is a risk of isolation of such 'non-Labex' teams, which may affect further development of internal research within the unit teams.

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

Strengths and possibilities linked to the context

RNA biology has exploded these last few years and revealed connections of RNAs to almost every aspect of gene regulation and to human diseases, highlighting the strong interrelationships between basic science, biotechnology and therapeutics, as it was recently observed with the Covid-19 pandemic and the development of RNA vaccines.

The ARN Unit is very well focused and has an excellent organisation around ten teams, each developing a distinct facet of RNA biology in disease. The last six-year period was marked with a move towards a more integrative biology from structural approaches to omics and microfluidics rationale, validated by supervising bodies and a Scientific advisory board. With this integrated scientific concept and cutting-edge methodologies, the unit provided an excellent stimulating research environment for both established and young scientists, and foster synergies between the teams. Several teams of the Unit use cutting-edge tools combining RNA structure biology and bioinformatics, microfluidic-based technologies, cryo-EM structure and dynamics of complex nanomachines, microcalorimetry and switchSENSE!. In general, this highlights the interdisciplinary nature of the research activities promoting excellent and durable interactions between the structural biologists, biophysicists, bioinformaticians, chemists, and biologists.

The outstanding adequacy between the unit internal organisation and its operational implementation of this strategy can be exemplified by the reunion of academic experts in all RNA field involved in disease. Indeed the unit represent an exceptional space containing leaders in regulatory RNAs encoded by viral (E01, E02, E06, E07, E08) and bacterial (E01, E04, E05, E09, E10) genomes, experts in characterisation of RNA modifications and their functions (E01, E02, E03, E09, E10), in translational control and decoding (E01, E02, E03, E07, E09, E10), in deep mechanistic studies of gene regulation (E02, E03, E05, E06, E08, E09), in the structural analysis of RNA machineries (E01, E02, E03, E06, E09, E10), and in the evolution of RNA and protein functions (E07, E10).

The Unit remains opened and flexible in order to integrate new emerging fields but also to respond to urgent societal needs (team E02 non-conventional translation initiation of the SARS-CoV-2 RNA).

Weaknesses and risks linked to the context

The committee did not observe any weakness in this aspect.

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

Strengths and possibilities linked to the context

The human resources management of the unit is excellent with great care in gender equality and non-discriminatory, in matters of training, internal mobility and careers development for its staff. For instance, the unit is integrated in the equality network of the Alsace Delegation of the CNRS since 2020 (2 equality referents in the unit; place of women at the CNRS) and uses the resources of the Equality-Parity-Diversity mission (University of Strasbourg). Referents detect sexist and sexual violence at work, and to be aware of equality during the recruitment process and the development of scientific and administrative careers (visibility on website; email, seminar on gender disparity 'Being a woman in the world of research in 2019 – 80 points of view', 'Archeosexism exhibition' in 2021; VIRAGE survey; survey on parity of genders).

The unit has an excellent organisation to monitor working conditions of its staff, their health, safety and the prevention of psychosocial risks (two Safety Officers, fire safety team members). The organisation of prevention of the Unit involves several aspects as notified in the internal regulations document of the Unit (medical monitoring, specific preventive measures, waste management, emergency organisation, conduct in the event of an accident, service accident, and safety trainings and personalised training for L2:L3, writing of the 'Document Unique' of the Unit. During the pandemic situation a continuity plan was set up and put the unit in a great position to react to emergency situation.

The Unit has an excellent provision for the protection of the scientific assets and computer systems by following the Information Systems Security Charter in force at IBMC (ie CNRS SSI Charter; and internal regulation document) and controlled by 2 CSSI officers (coordinated by the IBMC FR1589). Besides, the access to the Unit data can only be done from computers provided by the Unit.

The Unit has a very good risk prevention for environmental protection and the pursuit of sustainable development goals with one person in charge of communication and encouragement in these aspects to assess and reduce the carbon footprint of the unit (consumption of buildings; movement of all members, travels for missions and home-work journeys). A committee has been created involving the three IBMC Units in order to implement solutions to reduce carbon footprint on the environment (carpooling recycle paper, boxes, plastic, pens, batteries, and glass; minimise the use of plastic products; videoconferences).

Weaknesses and risks linked to the context

Since there is no incentive scheme for teams to improve their internal standard to reduce their environmental impact and footprint, there is a risk that real progress would reach a minimum plateau and would only depend on individual initiatives. In addition, the absence of gratification for the Environmental officer could also create a risk with time of decrease attractiveness for such a mission.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The unit has an exceptional attractiveness with an excellent visibility in France (locally with IdEx and several nesting networking and common organisation) and in Europe (hundreds of invitations to International meetings. The unit is excellent in recruiting young scientists from PhD to junior team leaders (45 PhD and 3 team leaders' recruitment). Finally, the capacity to attract funds (European, local or national as illustrated by three ERC, two labex, one equipex or 30 ANR among others). Annually, the Unit's overall budget is approximately €2 million (excluding salaries for permanent positions), 85% of which comes from external funding (excluding CNRS and the university) is exemplified by the excellent visibility and expertise of the platforms (in the unit or IBMC).

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

Strengths and possibilities linked to the context

The unit has an outstanding reputation with members of the unit regularly invited to present their work in academic institutions or at international and European congresses (350) and also with the unit, or members of the unit, organising major international and European congresses (12 international meetings). The unit invited 60 internationally renowned researchers for conferences. In addition, members of the unit hold editorial responsibilities and take part in research steering or scientific expertise bodies at international, European and national levels.

The unit has an outstanding recognition at the international level with members winners of various international, European and national scientific prizes and awards. For the scientific recognition, several members of the unit are in the editorial of scientific journals and editor of books/In terms of research management, some were nominated as members of CoNRS, Inserm, or scientific evaluation committee of the Pasteur Institute, or at high levels of decision at the University of Strasbourg. The Unit members also play important functions in national and international societies (French Society in Biophysics; French society for crystallography; committees of SFBBM; evaluators of specific programs of the European Commission or European committees; FEBS Fellowships Committee; member of Academia of Science; Academia of Science Leopoldina and Academia Europaea; AcademiaNet).

In terms of distinction and awards, the unit has an excellent to outstanding nominees (Chevalier de la Légion d'honneur ; Lifetime Achievement Award of the RNA Society, Prize of China Academia; Rolf-Sammet Award of Goethe Universität, Louis Pasteur medal of French Academia of Sciences Prix Niçoux).

Weaknesses and risks linked to the context

The committee did not observe any weakness in this category.

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

Strengths and possibilities linked to the context

The unit has an excellent environment and supervision for PhD (46 PhD, average 45.5 m) and only three did not yet published their work (2 PHDs have articles in BioRxiv) with mainly fellowships from the University of Strasbourg 'École Doctorale des Sciences de la Vie et de la Santé' and from the Graduate School IMCBio. A large proportion (35%) of PhD students are coming from various foreign countries (i.e. Europe, Lebanon, Mexico, India). All PhD students have a thesis advisory committee for their 'comité de thèse' and the Unit undersigns the 'Charte du doctorat'. Besides, all the teams regularly welcome students at the L3, M1 and M2 levels every year (around 10/year). Overall, 41 M2 students, and 160 students (including M1, L3, Erasmus, and technicians/apprentice-technicians) have been trained.

In the past six years, seven 'Habilitation à diriger les recherches' have been defended, leading to 27 HDR on a total of 31 tenured researchers. The unit also hosted 21 postdocs (13 national and 8 international) and 22 engineers. The students set up a club (regular meeting, introduce several scientists presenting seminars, share lunch and discussions; 'Monday seminars'; iGEM team of Strasbourg University gold medal).

The Unit hosted 8 scientists with a position at the University of Strasbourg (Unistra). Although they only represent 20% of the permanent researchers, they are involved in teaching and in many collective responsibilities.

The unit has an excellent visibility to attract junior and senior researchers (tenured positions). During the evaluated period, four junior scientists got a position (1 Inserm, 1 CNRS and 2 Unistra). One of them was awarded a JCJC ANR (MetalAureus, 2020) and an IdEx attractiveness funding. Two got a starting fund from Unistra allowing an ANR JCJC application. Two senior groups applied to start their team in the unit during the period showing the excellent visibility of the unit (2018 and 2019) with one finally accepting another position in Germany. The Unit also hosted several guest researchers for short periods of time from Japan, China and Israel.

The unit has excellent operational strategies to monitor research integrity and open science (all the publications in Hal and in UnivOAK (Unistra) databases with one person in charge). The unit developed the sharing of data management in each team following the FAIR data principle (Findable, Accessible, Interoperable, and Reusable). Two referents are in charge of the communication to the lay public. The director of the Unit presents at the beginning of the year the ethical rules that all members must take into account. The national charter of ethics is given to all members and to all incomers as well as the CNRS guide 'promoting honest and responsible research'. An attestation of knowledge of the information signed by each person concerning ethics is requested and kept in the Unit to guarantee that all the members of the Unit are aware of the ethics rules.

Weaknesses and risks linked to the context

While two PI expressed their interest to join the unit during the last term to create new senior teams with complementary technological and thematic expertise, they finally could not join having other opportunities elsewhere.

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

Strengths and possibilities linked to the context

The unit has an excellent to outstanding track record in international and European calls for projects with one ERC funding (2016–2021,) one ERC collaborative (2011–2017), one ERC starting grant (ERC STG 2017), two Marie Skłodowska-Curie fellows, and one ERA-Eurostars-2 (2018–2021), two Cost (networks Arbre-Mobieu and EPITRAN), one International Research Project (United Arab Emirates. four Bilateral financial supports (Procope with University Leipzig, University of Potsdam; Maimonide with University of Jerusalem; PICS with Pampelona University; FACE with University of Urbana; Hubert Curien with Zhejiang University)

The unit has outstanding implications in structures and projects funded by the 'Investissements d'Avenir' (PIA). (NetRNA LabEx 2011–2021, MitoCross LabEx 2012–2021, I2MC EquipEx 2018, and PIA3 (Graduate School IMCBio, Integrative Biology; IMCBio+ Interdisciplinary Thematic Institute, 2021–2029; InnoVec ITI, 2021–2029).

The Unit has excellent to outstanding success in obtaining projects funded by the National Research Agency (ANR) with 30 ANR to teams (17 as PI and 2 international; 3 ANR JCJC) or unit level (1 IdEx-consolidator, 4 IdEx-attractivity, 1 IdEx-USIAS-FRIAS, 4 USIAS) as well as with projects issued by the supervisory authorities, local authorities, from the region Grand Est (PhD contracts, projects, CPER) and from companies such as Adisseo, Sanofi, NovAliX, and Novaptech or charities as (4 FRM, 7 SIDACTION, 1 AFM, 1 ARSLA, 1 Ligue contre le cancer).

The unit has excellent capacity to fund doctoral and post-doctoral contracts, engineers and technicians, chairs and major equipment using its external contracts (85% of the total budget) allowing to acquire specific equipment (i.e. LC-MSMS for RNA modifications, switchSENSE, μ ITC) and recruit engineers. The NetRNA LabEx has provided a junior chair (2016) allowing hiring technical support, PhD fellows, and postdocs.

Weaknesses and risks linked to the context

The committee observed no weakness in this category. However, the international visibility through European or international networks remains an aspect of improvement within the coming years.

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

Strengths and possibilities linked to the context

The unit has excellent platforms with cutting-edge equipment demonstrators backed by a quality label or certification run by technical staff, including a large biophysic platform (DLS, X-tal controller, crystallization robot, vitrobot for preparation of cryo-EM grids, ITC advanced microcalorimetry, switchSENSE next-generation Biosensor and mass spectrometry). All equipment is managed by four highly qualified engineers on permanent positions. One team developed microfluidic devices applied to RNA biology with the financial support of the LabEx. The expertise of this team is unique in France but also at the international level in the field of droplet microfluidics applied to the evolution of RNA functions, the design of novel RNA biosensors or RNA aptamers.

Weaknesses and risks linked to the context

Given the high level of technical expertise within the unit and the cohesion of the IBMC and Strasbourg platforms, there is no weakness in this aspect.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The scientific production is of very high standard, with an excellent publication rate considering the structure and staff of the unit with a total number of citations of 6443 over the period and a total of 278 publications (including 9 BioRxiv, 29 involving more than 2 teams from the unit, 31 reviews and 71% as lead authors) in international journals (2 Science, 7 Nat Comm, or 3 EMBOJ and 1 Mol Cell among others). Most of the teams published at very high levels. Only three on the 46 doctoral students had not published their work when the thesis report was written.

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

Strengths and possibilities linked to the context

The unit has an excellent to outstanding scientific production with a total of 278 publications (including 9 BioRxiv manuscripts, 29 involving two or three teams, 31 reviews and 71% main authorships). The total number of citations for the period is 6443 with several in general journals (2 Science, 4 PNAS, 7 Nature Comm, 9 Scientific Reports, 3 EMBO J, 1 EMBO Rep, 2 Cell Rep, 1 Mol Cell, 2 Elife). Considering the size of each team, the scientific production is rather balanced, and the average citation is ~500/team for the period with publications important in their field of interest.

Weaknesses and risks linked to the context

The unit has an excellent track record of publications with 29 involving several teams of the unit but one team had difficulties with a low publication rate (numbers and visibility) over the last term. The risk is to see a funding income reduction and a drop of visibility.

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

Strengths and possibilities linked to the context

Considering the size of each team, the scientific production is very well balanced, and the average citation is ~500/team (for publications within the period). Several of these works can be grouped within 'Structure and specificities of the ribosome machineries in various pathogens and their hosts' (Team E01- RNA 2020; Team E02; Nature Comm 2016; Team E01/E11 Cell Rep 2020; Teams E11/E09 NAR 2020; EMBO J 2017), or under 'Identification of novel RNA machineries, RNA-based mechanisms and networks involved in stress responses, virulence, host-pathogen interactions and in human diseases' (Team E02, RNA 2021; E03 PNAS 2016; E04, PNAS 2020; E05 Nature Microbiol 2019; E06, NAR 2018; E08 PLoS Pathogen 2021; E09, EMBO J 2019; E07 J Virol 2020; E10, Nature Chem Biol 2020), and finally within 'development of novel technologies leading to major applications' (Team E04, LabCom DiagnOxi; E10 MicroOmics SAS 2021). The PhD contribution to the research is excellent, with only three PhD students over the period of evaluation without publication, but 2 uploaded articles in BioRxiv and one under revision.

Weaknesses and risks linked to the context

None

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

Strengths and possibilities linked to the context

The scientific production of the unit is the result of research activities that comply with all the rules and values guaranteeing that they are honest and scientifically rigorous. The Unit follows the national charter of ethics for the research professions and the 'Integrity and responsibility in research practices' guide. All the members of the Unit receive this document, and explanations are providing every year by the director of the Unit to all the new incoming persons.

The tracability of the work is very good with all members receiving a laboratory notebooks with a specific number registered. The notebook contains protocols and experiments and belongs to the Unit. Besides, robust protocols often validated by an engineer exist in each team. For the teams who have confidential results leading to patents or valorization, their books are signed and kept in a protected area when the persons are absent.

The scientific production of the unit respects the principles of open science by sharing publications, methods, data, codes and other elements of its scientific endeavour as broadly and as quickly as possible. The Unit has implemented the CNRS roadmap for Open Science. All the publications have been first deposited on Hal (CNRS) and then on UnivOAK (Unistra) databases following the FAIR data principle. All NGS data are deposited at NCBI's Gene Expression Omnibus (GEO), the mass spectrometry proteomics data are deposited to the ProteomeXchange Consortium. Many teams systematically upload their manuscripts to free preprint servers before publication, and the Unit encourages all members to publish in peer reviewed open access journals or to pay the fees for open access.

Weaknesses and risks linked to the context

None

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The Unit had an excellent promotion towards the non-academic interactions (hospitals, companies), and to generate products for the socio-economic world (13 patents, 1 startup 1 labCom). This result resides in excellent trainings by IMCBio+, InnoVec, and ED414 and illustrated by the activities of several teams (E01, E02, E04, E05, E06, E10). The communication towards the general public is regular thanks to two dedicated persons (Fête de la Science, videos, pictures and posters, organisation of events with schools, contest of crystallization, video RNA sketches, 'my thesis in 180 sec').

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

Strengths and possibilities linked to the context

These last years, technology transfer has been facilitated by internal training of the Unit members, including the PhD students with the help of IMCBio and Satt Conectus. Two PhD students (teams E06 and E10) have been awarded with the project 'Challenge your PhD' to define potential of the research to be transferred to private sector. Several teams (E04, E05, E08 and E09) have collaborative projects with hospitals (team E05-Pasteur Institute with a project on diarrhea caused by *Shigella*; Team E09-hospital of Lyon on Staphylococcal diseases; Team E04-invited member of the American Charity Cure for Congenital Muscular Dystrophy and contact with families).

Weaknesses and risks linked to the context

None

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

Strengths and possibilities linked to the context

The development of new technologies and discoveries with economic potential already led to patenting and technology transfers. In this respect, the director of the Unit is assisted by one of the PI, referent for the Unit, relaying information from the valorization offices of the CNRS, Unistra, and from Satt Conectus, to the different bodies of the unit (Unit Council, the Scientific Committee). Technology transfer has involved several teams (E01, E04, E05, E07, E08, E10) leading to thirteen patents, two invention disclosures, four (pre-) maturation projects, and to the development of the MicroOmix start up (team E10). With the help of the CNRS valorization office, several partnerships with companies have been established (E01-Sanofi-Cifre; Eurostars2; E02-NovAliX; E10-Novaptech). The LabCom DiagnOxi (E04) has been created and recently renewed in partnership between Adisseo company and CNRS (collaborative funding and a Cifre grant) to identify biomarkers sensing infectious and environmental stresses (diagnostic for adaptation and/or resilience to stresses).

Weaknesses and risks linked to the context

No weaknesses were identified in the strategy and means put together by the unit to promote the development of products for the socio-economic world. However, even though the number of patents and inventions are excellent indicators of a constant invention creativity and willing to transfer, the numbers of private collaborations, licensing of patents and start-ups creation are rather limited, with several projects that failed, essentially due to the lack of investors or chilliness of industrial partners. The risk is that several PI or inventors' candidates get exhausted in the process and finally would invest less time in these transfer activities.

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

Strengths and possibilities linked to the context

The unit has been involved in several and regular actions to increase its visibility in biology and infectious diseases for the benefit of the society through academic communications, open science and diffusion of information

towards the general public. Several staff members have been active during the Covid pandemic to explain RNA research, and the importance of basic science that led to the concept of RNA vaccines.

Weaknesses and risks linked to the context

None

C – RECOMMENDATIONS TO THE UNIT

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

The main recommendation is to take care of teams out of the Labex and ITI perimeters to find ways to include them especially within the IMCBIO doctoral school PhD program recruitment. This will help the integration of their expertise within the unit and limit their isolation. The unit has an excellent internal organisation but while novel missions appeared and need to be reinforced such as health/risk or environmental considerations/officers, they would benefit of personnel valorisations and teams' incentive programs.

Recommendations regarding the Evaluation Area 2: Attractiveness

The unit has an outstanding visibility in the RNA field. The lack of recruitment and the departure of a young team at the beginning of the term did not destabilize the unit, revealing its cohesion and stability. However, regular calls for young PI associated with an attractive starting package would compensate the natural turnover of the teams in the unit, a guarantee for durable and sustainable renewal of ideas, techniques and strategies while maintaining competitiveness for the future unit organisation. The international visibility through European or international networks remains an aspect of improvement within the coming years.

Recommendations regarding Evaluation Area 3: Scientific Production

As for many research organisations, one team has difficulty to publish regularly and/or in high-profile journals, over a long period of time. The recommendation is that the unit direction thoroughly assess whether the situation is transient or whether it could last for an even longer time. Unsolved situations might put at risk the group itself (or some members as PhD and Postdoc) and the research organisation with limited resources. The assessment might result in proposing merging activities with other complementary subgroups to reinforce, or alternatively to initiate transverse strategies to help these groups to publish through intra-unit collaborations with a clear and transparent time limit.

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

Although the unit has excellent strategies deployed to push their expertise in basic science to transfer towards the socio-economic world, the lack of clear success in start-ups creations or patent licensing might push the following recommendation: the clear opportunity of the geographical localization of Strasbourg is an excellent asset to develop partnership with the German socio-economic world and engineering activities. A recommendation would be to develop through a dedicated tech transfer project manager such strategies that might be seen in collaboration with the local Satt or independently.

RESPONSES TO SUPERVISING BODIES CONCERNS

NA

TEAM-BY-TEAM ASSESSMENT

Team 1: Structure and Dynamics of biomolecular machines

Name of the supervisor: Mr. Eric, Ennifar

THEMES OF THE TEAM

The research projects are centered on the functioning of the ribosome machinery in various pathogens, by combining state-of-the-art biophysical and structural approaches and molecular dynamics. Their goal is to understand the molecular mechanism of biomolecular machineries using an integrated biophysics approach, combining biochemistry, thermodynamics, kinetics, structural biology and molecular dynamics.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Previous weaknesses

The previous report highlights that the development of new methods has led to many collaborative studies (which is a good point) but may have weakened the development of in-house topics due to limited manpower. In this report, the team has increased its staff and continued to develop new technologies. This development has led to international collaborations and the production of joint publications. Finally, the previous report underlines that the team does not have a clear involvement in training activities. There is still no clear action on training.

Previous recommendations

The recommendation of the previous report was that the team should maintain a high level of research on internal biological topics. During this period, the team has maintained its high level of research on internal biological topics and has published seventeen papers in very high-quality journals. Secondly, the recommendation of the previous report was 'It could be beneficial for the team to negotiate contracts with partner companies.' During this period, the team concluded several partnerships with private companies, filed patents on this work and obtained financial support from the Satt. Finally, the previous report encouraged the team to participate in training activities on the use of ICT technology, but no real involvement in teaching was made.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	3
Scientist (Chargé de recherche, CR) and associate	2
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	3
Subtotal permanent personnel in active employment	8
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	0
Post-docs	0
PhD Students	2
Subtotal non-permanent personnel	2
Total	10

EVALUATION

Overall assessment of the team

The team includes eight permanent staff with strong expertise and methodological developments (biophysics, crystallography, structural bioinformatics), addressing the function of the ribosome in various pathogens. The team has developed excellent collaborations (14 contracts), maintaining a high level of production (17 articles) with an excellent visibility (organisation invitations to meetings) but lacks training and teaching activities (2 PhD only). Overall, the team has an excellent scientific output, developing new methods while addressing important biological questions.

Strengths and possibilities linked to the context

This is a well-established team with eight permanent members, five PhD students and two other personnel is on short term contracts. The team has a long-standing expertise in biophysics and structural biology and has been a pioneer for methodological developments.

The scientific production of the team is excellent with 21 articles as main contributors in very good to excellent journals (1 *Angewandte Chemie*, 4 *Nucleic Acids Research*, 5 *RNA*, 2 *Cell Reports*, *RNA Biology*, *ACS Infectious Disease*, *Journal of Medicinal Chemistry*, *Biochimie*, *Journal of The American Society for Mass Spectrometry*, *Journal of Chemical Information and Modeling*) and more than twenty collaborative publications including several papers in high impact journal (*NSMB*, *Angewandte Chemie*, 4 *Nucleic Acids Research*). Regarding the publications of the six doctoral students, three of them have published as first author in book series but a major article as first author is on hold due to patent application and/or involvement of industrial partners, two others have respectively one and five publications as first authors, while only one PhD student has not yet published as first author. However, all of them are co-authors of major publications of the team. The visibility of the team is excellent. Many collaborations have been established as attested by the number of collaborative publications. The two books edited by Eric Ennifar have reached an audience of several tens of thousands. Members of the team have contributed news and views (*Nature Chemistry*) as well as reviews (*RNA*) in high impact journals. The team is part of the European network Arbre-Mobieu.

The team has obtained over the years a number of regional, national or international fundings of limited amounts.

The non-academic activity of the team is excellent with partnership (including a Cifre contract) established with different industrial companies (Sanofi, Dynamic Biosensors, Novalix, Malvern Panalytical). Furthermore, members of the team are authors of two patents and have deposited a declaration of invention.

Weaknesses and risks linked to the context

The team is not involved in teaching activities, which could hamper its access to future PhD students. The team has recruited one post-doc during the period and has welcome one visiting researcher from Japan. The publication output of most PhD students is low.

RECOMMENDATIONS TO THE TEAM

The committee recommends that the team targets publications in higher-profile journals to increase the visibility of the research work.

The team may strengthen efforts to recruit national and international post-doctoral fellows.

The team may be more involved in teaching to attract more students and/or recruit assistant-professor(s).

The team should reinforce collaboration with other teams of the unit.

The committee advises the team to take advantages of their current network of collaborators to investigate the possibilities of obtaining more important national or international fundings.

Team 2: Evolution of translation initiation systems in eukaryotes
 Name of the supervisor: Mr. Gilbert, Eriani

THEMES OF THE TEAM

The research projects of the team are focused on the study of translation initiation in eukaryotes and more particularly on the characterisation of unconventional initiation mechanisms that use structural elements of the mRNA to recruit initiation factors and ribosomes. The team is also interested in the mechanism of initiation and translational recoding of selenoprotein mRNAs and the initiation of the SARS-Cov2 viral genome following the 2019 pandemic.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

During the previous evaluation, it was recommended to the team to focus on fewer projects and less collaborations in view of the size of the team and its low level of funding as well as to attract post-docs to improve its international visibility.

Two post-docs have joined the team (one in September 2020 and one in December 2021) and funding has been secured. The team has still many collaborations but this is a strong point that allows to expand their study models and secure many funding.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	3
Scientist (Chargé de recherche, CR) and associate	0
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	4
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	1
Post-docs	2
PhD Students	1
Subtotal non-permanent personnel	4
Total	8

EVALUATION

Overall assessment of the team

The team has an excellent to outstanding productivity with 24 publications over the period including articles in Nature Communications, Nucleic Acids research and Elife in key position with many collaborative studies. The team has obtained nearly 900 k€ of contracts over the period which is quite remarkable. Overall, this is an excellent to outstanding team, with excellent scientific output and visibility.

Strengths and possibilities linked to the context

The team has an excellent to outstanding productivity with 24 publications over the period including articles in Nature Communications, Nucleic Acids research and Elife in key position. Fifteen publications have corresponding authors coming from one or two of the three team leaders, including the PI. Nearly half of the articles are in collaboration.

The visibility of the team is excellent to outstanding with ten oral presentations and fifteen posters in international conferences over the period. The team has obtained nearly 900 kEuros of contracts over the period including a contract in partnership with the company Novalix (France Relance recovery plan), which is quite remarkable.

The main theme of the team has been enriched by two new study models (mechanisms of translation of Tau mRNA in Alzheimer Disease and SARS-Cov2 translation) which are funded, which reinforces the expertise of the team and its ability to attract collaborations.

The non-academic activity of the team is excellent.

Weaknesses and risks linked to the context

The dynamism of the team is mainly carried by two senior researchers, including the PI. The recruitment of future students could be a problem since the new university school of research in integrative molecular and cellular biology (IMCBio+) gives its priority to the three Labex INRT, MitoCross and NetRNA to which the team does not belong.

RECOMMENDATIONS TO THE TEAM

The leadership of the team has been mainly carried out by one of the senior researcher of the team and must be maintained. The distribution of responsibilities between the three senior researchers could be better balanced.

Team 3: Biology of tRNA and pathogenicity
Name of the supervisor: Ms. Magali Frugier

THEMES OF THE TEAM

The team research activity breaks down in two axes. The first one focuses on the study of translational regulation of protein synthesis and activity, in particular in malaria parasite Plasmodium, through its interaction with host cell via tRNA import machinery. The second one deals with the crystallography and the integrative structural biology through the development of new tools for the serial high-resolution structure monitoring of RNAs, proteins and their complexes and their biophysical characterisation. In addition, a translational research is carried out in collaboration with Australia hospitals on aminoacyl-tRNA synthetase mutations.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous Hcéres report highlighted that the work on GRS is not yet clear and recommended to develop a working hypothesis.

In the new report, this project was not mentioned, and was discontinued for the benefit of the new integrative structural approaches.

The previous report underlined that the collaborative work does not reach the same impact as the main projects; the grant funding is limited and the PI relies mainly on PhD and MSc students. It recommended more efforts on attracting post-doctoral fellows, collaborations and the increase of grant funding.

During the evaluation period the collaborative work of the team was quite active. Fruitful translational research was carried out in collaboration with the Australia Children's Hospitals on mutations in aaRs, giving five papers in high-rank journals. Several collaborations are carried out with synchrotron facilities, and with the leading Ln chemistry labs. Excellent common publications are obtained with German universities, as well as local partners IGBMC, IBMP.

However, only one post-doc was recruited for only 3.5 m, his work did not yet produce publications.

It was recommended to improve the communication to a broad audience.

The communication to scientific and lay public was considerable particularly on Plasmodium and structural biology. One team member is also the communication responsible of the unit and promotes very efficiently the innovative forms of digital communication.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	2
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	2
Subtotal permanent personnel in active employment	5
Non-permanent teacher-researchers, researchers and associates	1
Non-permanent research supporting personnel (PAR)	0
Post-docs	0
PhD Students	3
Subtotal non-permanent personnel	4
Total	9

EVALUATION

Overall assessment of the team

The work of the team is very original both in fundamental research on the structure and functions of the malaria parasite protein tRip, and in the domain of innovative technological developments in crystallography. Both axes have important translational potentials and constitute the basis for the growing number of national and international collaborations. The scientific production is appropriate to the size of the team and is of high quality. The team communicates regularly on its research to general audience, and is also strongly implied in PhD training and editorial and review activity.

Strengths and possibilities linked to the context

The team benefits the high international reputation in the field of structural and functional investigation of *Plasmodium* molecular machinery and its unique interactions with host cell tRNAs. After the discovery of tRNA import protein tRip, in the course of the evaluation period, it characterized in depth the important features of this protein (e.g. localization on the parasite surface, interaction with human tRNAs, functional importance in the process of their import to the parasite, etc) and discovered three aminoacyl-tRNA synthetases, that specifically interact with tRip and thus regulate MSC assembly. The structural know-how developed with tRip was successfully applied to two tRNA maturation enzymes, that was valorized in the frame of local (IBMP) and European (Leipzig) collaborations. The scientific production of the team during the evaluation period was excellent with fourteen original papers (PNAS 2016, JBC 2017, PLoS ONE 2018, PNAS 2019, NAR 2021) and reviews and ten collaborative publications in high-rank general (e.g. NAR 2017, NAR 2019, PNAS 2020) and specialized journals.

The team was attractive enough to be joined by the highly qualified staff (research director 2016, and research engineer 2018). It develops the new promising microfluidic chips dedicated to the serial crystallization and X-ray analysis of biomolecules. In this highly competitive field, their ChipX slides take advantage of the counter-diffusion of solutions, and were tested with novel Tb nucleation agent to produce the high-quality X-ray diffracting and even neutron-diffracting crystals at room temperature. The exciting envisioned application of this new technology is the time-resolved structural analysis of enzymatic reactions, however yet to be

demonstrated. The valorization potential of this development is being evaluated with the CNRS IP department, that would give the opportunity for the team to proceed the technology transfer and establish more sound relations with the socio-economic partners.

The important know how of the team in the biophysical crystallography is the basis for collaboration with industrial Xtal Concepts, and contribution to MBioFaSt facility. The team communication to the lay audience and scholars is very good to excellent in traditional media (videos, posters, pictures) as well as novel digital communication and teaching forms (e.g. VR 3D films), Fête de Science, organisation of the academic contest of crystallization.

The team's members are involved in teaching activities Master course and organisation of summer school. Both research directors of the team are members of the scholarship and pedagogic boards of the doctoral school of Unistra. This involved may contribute to the high number of PhD student in the team.

Weaknesses and risks linked to the context

There is no obvious scientific weakness of the team.

However, the two main research axes of the team seem to feature independent and parallel evolution. Their synergy is not yet clearly demonstrated, for example by applying the advanced integrated structural approaches to decipher RNA-protein interactions in *Plasmodium* translation machinery.

Such 'bicephale' functioning of the team could lead in fine to the risk of divergent scientific objectives and trajectories. The announced departure for the actual team leader to join another team of the unit, confirms this risk, and necessitates profound reorganization of the scientific axes and orientation.

In spite of the numerous international and national collaborations and the good previous fund raising capacity, the team faced several unsuccesses in ANR calls and did not invest enough in post-doctoral recruitment. This could be partly explained by the pandemic lock-down condition in the second part of the evaluation period, but was already underlined by the previous Hcéres report.

The translational activity of the team in its main research axes seems not to reach the same level of significance as the scientific achievements.

RECOMMENDATIONS TO THE TEAM

The committee recommends to reinforce the efforts in recruiting national and international post-doctoral fellows. This should be facilitated by the recognized international leadership of the team in both fundamental research on Plasmodium ARN machinery and in the applied field of biophysical crystallography or microfluidics.

The interaction between the two main research axes (joined in 2018) should be clarified and their synergy better demonstrated if the team is maintained in its actual configuration. The interaction between them should be clarified and their synergy better demonstrated if the team is maintained in its actual configuration.

The team is encouraged to produce more efforts in exploring the valorization potential of its the scientific results. The discussions with Satt concerning the ChipX technology may be suggested. The druggable potential of the tRip activity may also be more taken in focus.

Team 4: Post-transcriptional regulation and nutrition

Name of the supervisor: Mr. Alain Lescure

THEMES OF THE TEAM

The team contributed to the development of specific biochemical and structure-function strategies to better decipher the biological role of the Selenium and its importance in health. In particular, they study the function of SelenoN, a protein linked to an inherited form of muscular dystrophy.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Previous recommendations:

It appears that the work on SelN proteins has been secondarily prioritised in order to set up the establishment of the LabCom. This may correspond to the development of a new axis of research, but the team must take care of dispersion for the Diagnosi project;

The team would benefit from increasing its international visibility. This may attract post-docs and probably also national and international funding.

The team should make sure that the contracts with industrial partners do not hamper the timely publication of the results. Otherwise, the team is at risk of losing attractiveness for academic research.

The team has to focus on some projects because of the potential dispersion that could occur from the private company involved in the LabCom, and also from the nature of the projects themselves.

The team did not address these recommendations. In contrary, the team further followed his partnership with Labcom, putting at risk the publication level (one student without a paper) and still lacks of visibility with no post doc in the team.

WORKFORCE OF THE TEAM

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

EVALUATION

Overall assessment of the team

The team has a fair publication record over the period (1 collaborative publication in PNAS, 2021, 1 review, 1 bioRxiv pending since 2018). Recent breakthroughs in the purification of the Selenon protein by the team and collaborators, raised expectations in moving forward structural and in vitro biochemical studies. The LabCom initiative has opened very good opportunities to study stress activation with genome wide approaches on different organisms (securing 263k funding up to end of 2023). The team lacks visibility and remains quite modest in size (2 PhD, 1 tech, 1 MCU, 1 CRCN).

Strengths and possibilities linked to the context

The team secured 263 k€ through a private collaboration. The visibility of the team is good to very good, with the PI invited in seven conferences and five lectures during the reporting period.

The team (mostly the PI) has good impact in the research structuration being one of the two corresponding scientists for the access to FR 1589, EquipEx I2CT, IBMC and also for the Imaging platform (IBMP). The PI participated in the organisation of the Esplanade Microscopy and Imaging platform directed by J. Mutterer (IBMP).

The team (mostly the PI) ensured very good activities in research organisation (Deputy President of the scientific committee at university institution) and members of different recruitment/evaluation committees (ESB, CNRS, Biovalley, Pole BMS University of Lorraine, programme Idex Attractivité, Telethon-Italy, Dim1 Health Ile de France) and reviewers of journals.

The team has reported inclusion in the society through actions with associations linked to Congenital Muscular Dystrophy and with the operation DECLICS.

Weaknesses and risks linked to the context

The team has a fair production with five publications during the reporting (1 main, 2 reviews, 1 collab and 1 main in bioRxiv) and one patent in 2020 with the LabCom. In the mean while the team had an uneven level/frequency of publications with one PhD student of the team who did not publish his work since 2017.

The team has weakness in attractiveness with no post-doctoral recruitment during the period.

RECOMMENDATIONS TO THE TEAM

It is recommended that the team identifies rapidly other PI(s) to develop collaborative and alternative structure-function research and secure future joint publications and increase visibility. This will help diversifying the team funding capacity and protect students' production. The inclusion of the team as a subgroup of a larger team might also have beneficial results for the unit maintaining the unique and original expertise of the group in the unit perimeter.

Team 5: Pathogenesis of bacterial infections and immunity

Name of the supervisor: Mr. Benoit Marteyn

THEMES OF THE TEAM

The team investigates the physiopathology of *Shigella*, a pathogenic enterobacteria responsible for the bacillary dysentery. Three main axes are developed: the role of oxygen and antioxidant molecules in the interaction between *Shigella* and host cells, the characterisation of the infection process at molecular and cellular levels and clinical studies to explore parameters that modulate the risk of diarrhea.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

not applicable

WORKFORCE OF THE TEAM

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

EVALUATION

Overall assessment of the team

This is a young team that has been successful over the period to perform and publish ground-breaking work in highly cited journals, to secure fundings and to attract collaborators in recent years. The research performed by the group is excellent.

Strengths and possibilities linked to the context

Considering its size, the team has an excellent scientific production over the current period of review by producing 21 publications, including papers in Nature Microbiology, Cell Chemical Biology, Immunol Cell Biol,

Matern Child Nutr, Scientific Reports, Blood, seven papers obtained in collaborations and reviews. The team develops a combination of complementary studies to characterize the infection process by Shigella, the adaptation of neutrophils and the effects of various parameters on the risk of diarrhea associated with the bacillary dysentery. The team has a number of equipment allowing experiments in anoxic or hypoxic environment, performs molecular and cellular analyses of the infection process.

The team has an excellent visibility and recognition in the field. It has been successful in getting funding (ANR JCJC, ANR PRC, USIAS fellowship), attracting students (4 PhD students) and two foreign postdocs, establishing international collaborations and by publishing a number of reviews (Cell Microbiology, Trends in Microbiology, International Journal of Molecular Sciences, Microbes and infection, Front Cell Infect Microbiol).

The non-academic activity of the team is excellent; one patent protecting the Myelotraker marker has been licensed to a company and the group is directly involved in clinical studies.

The contribution of the group for outreach activities has been limited because of the investment to secure fundings and long-term development of the team.

Weaknesses and risks linked to the context

The main weakness of the team is its small size. Another potential weakness is the absence of interactions with other groups from the unit or the institute.

RECOMMENDATIONS TO THE TEAM

The team should maintain its strategy of reinforcing the group by recruiting new collaborators and implementing original projects. It should develop as much as possible collaborations with other groups from the ARN unit and IBMC.

Team 6: Viral ribonucleoproteins, incorporation of the genome and assembly

Name of the supervisor: Mr. Roland Marquet and Mr. Jean-Christophe Paillart

THEMES OF THE TEAM

The team is an internationally recognized expert in the structural analysis of large RNA molecules and is developing innovative methodological approaches to study retroviral genomic RNA packaging including HIV, FIV, MPMV, MMTV and Influenza A viruses as well as how HIV Vif protein counteracted the function of APOEC3G/3F restriction factors.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

During the previous evaluation, it was recommended to try to obtain larger grants to recruit more post-docs. There is only one post-doc who arrived in 2018 but the participation of the team in the European consortium ITN VIROINF should open new recruitment perspectives.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	3
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	2
Subtotal permanent personnel in active employment	6
Non-permanent teacher-researchers, researchers and associates	1
Non-permanent research supporting personnel (PAR)	1
Post-docs	1
PhD Students	6
Subtotal non-permanent personnel	9
Total	15

EVALUATION

Overall assessment of the team

The team is internationally recognized for its work on HIV and Influenza genome packaging and many teams learn and benefit from their expertise in RNA structure methodologies. The visibility of the team is outstanding with their involvement in the European consortium VIROINF, their long-term collaboration with the United Arab Emirates University which will be further reinforced in the future and the french-german doctoral college between Strasbourg and Hamburg Universities coordinated by one on the senior scientist of the team. The overall level of the team is excellent to outstanding.

Strengths and possibilities linked to the context

This two-headed team is internationally recognized for their work on HIV and Influenza genome packaging.

The team's level of publication over the period (42 publications) is excellent to outstanding with 29 articles with at least one main author (first, last and/or corresponding) including papers in NAR, RNA biol, J. Mol. Biol. and Viruses. The team has a strong editorial involvement and several team members have been asked to write analyses and reviews (guest editors) for the Journal Viruses, mBio and Frontiers in Cellular and Infection Microbiology.

The visibility of the team is outstanding. The team is well funded with many national (ANRS, ANR, Sidaction) and international (VIROINF, ANR-DFG, IRP CNRS UAE) grants. One of the PI has a long-standing and fruitful collaboration with the United Arab Emirates University (9 publications during the evaluated period) which will be reinforced in the coming years by a new CNRS-United Arab Emirates University partnership. The team contributed to the foundation of a French-German Doctoral college in partnership with the University of Hamburg. The team's involvement in the European consortium ITN VIROINF is remarkable and can only reinforce the already outstanding attractiveness and visibility of the team.

The non-academic activity of the team is very good to excellent. The application potential of the team's research is strong and contacts have been made with a French Big Pharma via the Satt Conectus (improvement of the production process of influenza A vaccines), but unfortunately it did not go any further.

One of the PI is currently Deputy Director of the Unit and will become its Director for the next five years.

Weaknesses and risks linked to the context

There is no obvious weakness of the team.

RECOMMENDATIONS TO THE TEAM

One of the 2 PIs will become director of the Unit. It is important to secure the team structure in light of these future responsibilities.

Team 7: Retrovirus and molecular evolution
 Name of the supervisor: Mr. Matteo Negroni

THEMES OF THE TEAM

The team has a long-standing expertise in molecular evolution applied to the biology of HIV replication. During the time period, the team has focused on three main aspects: The evolution of the HIV pol (*integrase*) and env genes as well as the HIV long terminal repeats (LTR) that revealed key determinants under selective pressure; the use of original lentiviral systems to force evolution of genes relevant to anti-cancer therapy; the development of gene transfer lentiviral vectors for gene therapy.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Several previous recommendations have been suggested:

—*to put higher priority to the biotechnological goals of the team, which look promising for future applications. This aspect is difficult to evaluate. No publications are available due to intellectual property reasons.*

—*to seek more international exposure.*

The team is already internationally recognized for its work on molecular evolution and the team was part of an ERC grant until 2017. The team, however, did not attract international postdoc during the time period.

—*to continue strong engagement with both science community and general public and to seek closer collaboration with the biotech sector to exploit the promising dCK technology.*

The team is clearly engaged in science communication. Concerning the development of the team with the biotech sector, contacts has been made with the help of the Satt branch without any clear achievements yet.

WORKFORCE OF THE TEAM

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

EVALUATION

Overall assessment of the team

The team published a fair number of scientific papers, with six publications with leading positions (including 3 reviews) and three publications from collaborative works. All team publications referred to the HIV evolution axis. Publications concerning the biotechnical axes with translational potential are delayed for intellectual property reasons.

The publication record is good considering the modest size of the team (1 DR2, 1 MCU, 1 IE and 2 PhD). The overall level of the team is very good to excellent.

Strengths and possibilities linked to the context

The team obtained several grants (ANRS, Sidaction, Ligue cancer, Idex) for a total of 380k€ showing a good capacity of getting national funds.

All PhD students who defended their thesis have published more than one article as first author, and each of the present students already wrote a scientific review.

The team PI is active in term of scientific communication for non-scientific public (3 press releases, conferences on HIV evolution and videos), is involved in evaluating national and European grant applications, and participated to the edition of scientific papers in Frontier journals.

The team has a strong application potential and is in the process of raising funds or the creation of a start-up based on lentiviral vector production.

Weaknesses and risks linked to the context

The attractive technology of gene evolution based on infidelity of DNA synthesis by the HIV reverse transcriptase awaits for new results and development. The lack of publication on this aspect since 2015 due to intellectual properties (1 patent in 2017) is at risk for the recruitment of international student and postdoc and for grant obtention.

RECOMMENDATIONS TO THE TEAM

The team should maintain focus on the biotechnological and translational aspects of its projects (axes 2 and 3) which require funding and visibility to attract postdocs

Team 8: Non coding RNAs and viral infections
 Name of the supervisor: Mr. Sébastien Pfeffer

THEMES OF THE TEAM

The team has an internationally recognized expertise in microRNAs that control viral infection. The main focus of the team is to understand the regulation of viral microRNA biogenesis by identifying key RNA-binding factors using proteomic approaches. In parallel, the team is developing novel approaches (loss of function genetic screens and proteomics on double-stranded RNA) to dig out general principles of RNA sensing in antiviral innate immunity.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Previous recommendations emphasised on targeting key priority projects to raise even further the quality of the team publications. In addition the committee recommended create partnership with some Pharma industry to explore possible interest and potential collaborations and raise some concern on first author publication for postdocs.

The team has an excellent response to these recommendations since they certainly raised their international visibility with an ERC consolidator award (2015) and high-level publications during the period. No potential collaborations with Pharma were initiated at the time.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	4
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	1
Post-docs	0
PhD Students	4
Subtotal non-permanent personnel	5
Total	9

EVALUATION

Overall assessment of the team

The team had an excellent publication activity with seventeen articles and an excellent visibility with more than 4000 citations (including publications before this evaluation period), several organisations of meetings and the ERC consolidator award. The team has a very good involvement into structuring and evaluating the research with regular participations in manuscripts/grants reviewing, and in university/unit councils. The team and the PI have a good teaching activity (occasional lectures and 8 PhD trainings) and has recruited an assistant professor in virology.

Strengths and possibilities linked to the context

The team has an excellent publications quality rather than quantity with seventeen articles (including 4 reviews) in high – profile journals (several NAR), which have been cited 232 times (for a total 4623 citations all articles).

Since the last evaluation, the team has developed state-of-the-art technical approaches (proteomic on viral RNA templates, CRISPR/Cas9- mediated genome editing) and made significant discoveries such as the interplay between Dicer and PKR in Sindbis virus antiviral activity (Plos Pathogen, 2021), the identification of RNA-binding factors regulating microRNA (NAR, 2016) microRNA modulating Sindbis and HCV infections (J. Virol, 2020, Gut 2020) among other publications.

The team has an excellent visibility with organisations of meetings (Inserm Workshop; 2 CNRS thematic schools) and Oral presentations in international meetings (15 selected invited talks/seminars).

The PI has a very good activity in shaping research (PI in the Council member of UPR9002 and was a Strasbourg University faculty member). The team is involved in international grants evaluations (ERC, DFG, Polish NCS, BBSRC, MRC), the PI has been editor in two journals (PLOS One and non-coding RNA) and Reviewer of manuscripts for high impact journals.

The team has a good non-academic activity with regular communications using social media and several public outreach actions.

Weaknesses and risks linked to the context

The team currently lacks a long-term funding support (1 international ANR grant).

RECOMMENDATIONS TO THE TEAM

Extra care should be put into securing national and international grants, probably through collaborative applications.

Team 9: mRNAs and regulatory RNAs in bacteria
 Name of the supervisor: Mrs. Pascale Romby

THEMES OF THE TEAM

The team aim to define the mechanism of RNA-dependent regulation in bacteria and how post-transcriptional regulation impacts bacterial physiology. The team performs deep mechanistic analysis on the roles played by the RNA structures on the gene regulation and RNA-based regulatory networks within *Staphylococcus aureus*. The team uses a combination of in vitro and in vivo approaches, from chemical mapping of secondary structures and interactions to genetic manipulation of *S. aureus* strains and vectors.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

On the prior evaluation, it has been suggested that the team could have more applied applications, should maintain its level of implication in training and maintain efficient leadership of the team, and should concentrate on its core activity and scientific priorities with External funding.

All recommendations were followed with high success in external funding and high publication levels. The leadership has not been affected.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	2
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	5
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	0
Post-docs	1
PhD Students	4
Subtotal non-permanent personnel	5
Total	10

EVALUATION

Overall assessment of the team

The team has an excellent to outstanding publication record with 32 publications (including 1 EMBOJ, 1 Elife, 5 NAR, 2 RNA Biol, 1 Ann Rev Micro, mBio, Molecular Microbiology, 2 BioRxiv and 4 book chapters) for a total of 555 citations. The team has invested in new approaches including global methods to define the RNA targets of a specific regulatory RNA, to identify RNA interactomes, to monitor translomes in *S. aureus*, to characterize RNA modifications by mass spectrometry, and to identify the targets of RNA-binding proteins including ribonucleases.

Strengths and possibilities linked to the context

The team published excellent publications with 70% of the papers as main authors in the best journals of the field and excellent collaborative publications with other teams in the unit (Biochimie, NAR, Molec Biology and 1 BioRxiv). The team has an excellent funding capacity with several ANR, IDEX and FRM grants during the last period.

The team has an outstanding visibility with the PI and several members being invited and organizing conferences, lectures and seminars (13 organized, 17 invited) and also hosted several international visitors (4 prof, 2 PhD, 4 postdocs).

The team members have outstanding participations in evaluating science, being members of several organisation boards (Unit director, CSS1 Inserm, Co-Dir LabCom, Fondation Rottshild, HCERES committee chair), and scientific journals editors (Frontier in Molecular Biosciences, Microbiology, RNA Biol, Pathogens and diseases, Biochimie, Virulence, F1000, NAR and PloS Genetics) or SAB (I2BC).

The team has a very good to excellent teaching activity (1 Associate professor) and all participated in several PhD jurys, HDRs.

The team and its members received several awards (PEDR, 3 PhD award, 1 SFBBM publication of the year, Louis pasteur award, academia of sciences, academiae europae, academia net).

Weaknesses and risks linked to the context

None

RECOMMENDATIONS TO THE TEAM

Maintain the remarkable level of production.

Team 10: Digital Biology of RNA
Name of the supervisor: Mr. Mickaël Ryckelynck

THEMES OF THE TEAM

The team is a specialist in advanced high-throughput screening with droplet microfluidics applied to RNA engineering. It is particularly interested in development of new generations of fluorogenic RNA aptamers for cell imaging, up to single molecule, and the technology transfer of innovations. Besides, it studies fundamental biological mechanisms of eukaryotic ribosomes and viral IRES elements. It combines the expertise in microfluidic-assisted screening, molecular biology, bioinformatics, and deep-learning.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous Hcéres report noted that the academic reputation of the team is strongly based on the former team leader, and recommended the continued involvement of the previous team leader to assure the smooth transition.

The former team leader holds the title of emeritus professor, and is strongly involved in research activity. He contributed to the excellent scientific record of the team. He co-authored 36 peer-reviewed papers and one book chapter during the evaluation period, was invited to numerous national and international meetings, in particular as a keynote speaker until the end 2017.

It was also stressed the weak engagement with the lay public.

During the evaluation period the team partially addressed this issue by co-producing two documentary films about microfluidics and synthetic biology, a methodological paper and a national presentation of 'My thesis in 180 seconds' (Alsace award). However, more involvement in communication is expected, given the strong scientific recognition of the team.

It was recommended to make sure that resources of the team are not spread too thinly between collaborative projects rendering the team less competitive and preventing the new team leader from developing his own program.

The excellent scientific production of the team (> 50 papers), technological innovations and transfer (1 start-up created, 2 industrial collaborations), good fund rising capacity (1.45 M€ over 6 years) witness that this recommendation was followed.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	1
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	0
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	2
Subtotal permanent personnel in active employment	4
Non-permanent teacher-researchers, researchers and associates	1
Non-permanent research supporting personnel (PAR)	0
Post-docs	1
PhD Students	3
Subtotal non-permanent personnel	5
Total	9

EVALUATION

Overall assessment of the team

Considering its size, the team has been very successful over the current period of review by developing innovative technologies and methodologies, producing several articles in high-profile journals, obtaining contracts, filling several patent applications and developing entrepreneurs' activity. The research performed by the group is excellent to outstanding.

Strengths and possibilities linked to the context

The scientific production of the team is excellent to outstanding with eleven articles published in high impact journals including Nat Chem Biol (2 papers), Nature Com., Nucleic Acids Res., RNA, Methods (2 papers), Biochemistry, Micromachines, leading to 527 citations of the papers published in the period. The team develops very innovative tools and methods to construct and exploit different types of aptamers with specific properties. The team identified molecules belonging to a new generation of ultrabright RNA probes and biosensors. The visibility of the group is excellent to outstanding and the PI is recognized internationally as attested by invitations to international meetings (6 invitations in the period) or to give conferences in international institutes (2 invitations). The team leader is head of the Biochemistry Department of the University. Four PhD students have defended their thesis during the period. The team was successful in 6 ANR calls over six-year period. The non-academic activity of the team is outstanding; the PI has cofounded one startup and established a contract with another one, seven patents were accepted.

Besides the activity of M. Ryckelynck, the former PI has contributed 36 peer-reviewed papers, one book chapter and was invited to ten international meetings until 2017.

Weaknesses and risks linked to the context

The team has a small size and the PI has important teaching activities. One assistant professor has been recruited. PhD and post-docs constitute the main working force of the team.

Considering the potential of the technologies and methodologies developed by the team, we may expect more collaborations with other members of the unit or institute.

RECOMMENDATIONS TO THE TEAM

The team should maintain its strategy of implementing innovative projects and reinforce as much as possible collaborations with other groups from the ARN unit and IBMC.

CONDUCT OF THE INTERVIEWS

Date

Start: 20 October 2022 at 8:30 A.M.

End: 20 October 2022 at 5 P.M.

Interview conducted: online

INTERVIEW SCHEDULE

8:30 Test Zoom connections

8:35 – 8:45 Committee + CS (if needed)

<https://hceres-fr.zoom.us/j/97424434163?pwd=OVdCLlR6OVNkZ2VleHVpWTJlSTlAeXZ09>

Sessions scientifiques

<https://hceres-fr.zoom.us/j/92086255461?pwd=QVhBTlh3ks5MC1VaVRIvUjH5SWV4QT09>

8:45 - 8:55 Introduction / Presentation of the Committee members

9:00 – 9:25 Unit presentation by the DU (15'+ 10' discussion)

9:30 – 10:50 4 Teams (10' + 10' discussion) (Teams 1, 10, 2, 3)

9:30-9:50	Team E01: Structure and Dynamics of biomolecular machines	E. Ennifar, DR1 CNRS
9:50-10:10	Team E10: Digital Biology of RNA	M. Ryckelynck, PU2 UNISTRA
10:10-10:30	Team E02: Evolution of Translation initiation systems in eukaryotes	G. Eriani, DR2 CNRS
10:30-10:50	Team E03: Biology of tRNA and pathogenicity	M. Frugler, DR2 CNRS

Break (10')

11:00- 13:00 6 Teams (10' + 10' discussion) (Teams 4, 5, 6, 7, 8, 9)

11:00-11:20	Team E04: Post-transcriptional regulation and nutrition	A. Lescure, CRCN CNRS
11:20-11:40	Team E05: Pathogenesis of bacterial infections and immunity	B. Marley, DR2 Inserm
11:40-12:00	Team E06: Viral ribonucleoproteins, incorporation of the genome and assembly	R. Marquet, DR1 CNRS JC Paikart, DR1 CNRS

Break (5')

12:00-12:20	Team E07: Retrovirus and molecular evolution	M. Negroni, DR2 CNRS
12:20-12:40	Team E08: Non coding RNAs and viral infections	S. Pfeffer, DR1 CNRS
12:40-13:00	Team E09: mRNAs and regulatory RNAs in bacteria	P. Romby, DRCE CNRS

13:15-14:00 **Lunch break/debriefing committee, if needed**

14:00 – 14:30 Meeting Committee with Supervising bodies (CNRS, UNISTRA)

<https://hceres-fr.zoom.us/j/91328067836?pwd=MLkxQnBoSjZkdVBDYWpxQXlralhArz09>

Interviews

<https://hceres-fr.zoom.us/j/98755158227?pwd=NU5hc2Ulc3VYc2xRajJPbUJldDWFhEz09>

14:30- 15:00 Meeting w/ technical staff

15:00– 15:30 Meeting w/students

15:30– 16:00 Meeting w/researchers and EC (no team leaders)

16:00- Discussion Committee – DU

<https://hceres-fr.zoom.us/j/97424434163?pwd=OVdCLlR6OVNkZ2VleHVpWTJlSTlAeXZ09>

Committee/Report briefing

PARTICULAR POINT TO BE MENTIONNED

Excellent participation rate of all staff categories and profound statistical summary of the responses to the previously submitted committee questions allowed a vivid discussion in spite of Zoom meeting format and frequent problems with the sound volume and computer communication.

GENERAL OBSERVATIONS OF THE SUPERVISORS



Architecture
et Réactivité
de l'ARN



Strasbourg, le 14/03/2023

Dr Pascale Romby
Directrice UPR 9002

General Observations on HCERES report

To whom it may concern,

First of all, we would like to thank the HCERES committee for their thoughtful comments and recommendations on the general organization of the Unit, and for their appreciations on the teams' results. However, we would like to add clarifications on some of the criticisms/recommendations made by the committee as detailed below.

CHARACTERIZATION OF THE UNIT

PAGE 10 - EVALUATION AREA 1 "Since there is no incentive scheme for teams to improve their internal standard to reduce their environmental impact and footprint, there is a risk that real progress would reach a minimum plateau and would only depend on individual initiatives. In addition, the absence of gratification for the Environmental officer could also create a risk with time of decrease attractiveness for such a mission. "

The CNRS provided salaries bonus for the CNRS officers who oversee the health and the safety and for radioactivity protection. This is not yet the case for the environmental officer as for many other functions such as training, equality-parity, communication, informatic security, etc. The director considers the responsibilities that are not gratified for the distribution of the annual salary bonus to the engineers and technicians. However, such gratification cannot be attributed to the CNRS scientists who take care of the sustainable development or other activities. Noteworthy, numerous members of the unit are involved daily in various aspects of sustainable development activities, i.e. minimizing energy consumption, strategies for recycling various wastes and products. We are nevertheless aware that there is a risk with time of decrease attractiveness if the CNRS administration does not provide specific funds due to the costs of several actions, i.e., recycling of polystyrene. This cannot be done solely at the level of a single unit. This is why this activity is coordinated at the level of the institute in links with our institutions.

PAGE 15- RECOMMANDATIONS TO THE UNIT REGARDING EVALUATION AREA 1. "The main recommendation is to take care of teams out of the labEx and ITI perimeters to find ways to include them especially within the IMCBio doctoral school PhD program recruitment. This will help the integration of their expertise within the unit and limit their isolation."

The labEx NetRNA "Regulatory RNAs networks in response to biotic and abiotic stresses" gathers 11 teams from three different CNRS units (ARN, M31 in IBMC and IBMP). Initially it was aimed to decipher

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the functions of the non-coding genome across kingdoms, focusing primarily on regulatory RNAs and their machineries involved in infectious diseases. The project of NetRNA has evolved to generate an integrated view of the RNA-based strategies developed by pathogens and their hosts during infection and on the insect strategies to resist viral infection. As mentioned in the auto-evaluation report, the added value of the labEx to the unit was at different levels: 1) to reinforce the existing facilities (proteomics, genomics and HTS, mass spectrometry applied to RNA) used by all the teams of the unit; 2) to promote collaborations between the units of IBMC, IBMP, IVH, GMGM and IGBMC, and to induce funding leverages (even for the teams outside the labEx); 3) to introduce novel and unique expertise on Strasbourg site, useful for the community and the unit (i.e., microfluidics applied to RNAs (team E10), mass spectrometry applied to RNA modifications). The labEx has also contributed to the biophysical facility MBioFaSt headed by team E01 (i.e., participation to the acquisition of the dynamic Biosensor DRX2400). As it was mentioned in the auto-evaluation report and to all PIs of the ARN unit, the labEx NetRNA will expand over the next years by providing funding resources for PhD students to support new projects and new pathosystems to continuously generate new opportunities and challenges. This call was only addressed to the teams of the three units (ARN, M3I, IBMP) that were not yet partners of the labEx. This year, two PhD fundings have been attributed after oral presentations, and one of them was attributed for the team E06 (i.e., SARS-CoV2 packaging and consequences on host immune responses). This call will be renewed in 2023 and most probably in 2024. As the direct consequence, the additional teams will join the Graduate School IMCBio and will have the possibility to welcome IMCBio M1 students for 2 months-internships. To date, the Graduate school trained around 20 M1 students/year for all the community within ITI IMCBio+ (around 70 teams) and should expand in the coming years giving the possibility to the teams outside of the labEx to get funding supports for M1 internships. Finally, the labEx NetRNA will provide a package (450 k€, 3 years) to recruit a new team for the ARN Unit through an international call. Therefore, the HCERES recommendation is already put in place. Besides, the various teachers-researchers of the unit are all concerned and aware to attract the best students in the unit. They often invite researchers to provide oral presentations and courses at different levels. All the teams have trained many students over the period of evaluation. Although alternative strategies can be organized to attract even more students (at the national and international levels) to the unit (i.e., open IBMC day, symposium organized for and by the students, summer school...), there is however little risk that a team will be completely isolated in the unit.

TEAM-BY-TEAM ASSESSMENT

Team E01: Structure and Dynamics of biomolecular machines

1- « *The team may strengthen efforts to recruit national and international post-doctoral fellows* ». The team has already taken into account this recommendation as three international postdocs have been recruited in 2023 due to successful funds.

2- « *The team may more involved in teaching to attract more students and/or recruit assistant-professor* ». The activities of the team in teaching were missing in the appendix of the auto-evaluation report. However, most of the team's researchers are voluntarily involved in teaching and often respond to the requests for teaching from professors/assistant professors of UNISTRA. Members of the team created in 2022 a CNRS training course for "CNRS formation enterprises". Regarding the recruitment of assistant professors in the team in structure biology and biophysics, the team is obviously dependent on decisions taken at the faculty of Life Sciences and then at UNISTRA. A scientific council of the faculty where the directors of the units are present, select the research profiles based on the teaching profiles that are then discussed at UNISTRA council.

3- « *The team should reinforce collaboration with other teams of the unit.* » The team is considered as one of the transversal team of the Unit because (1) it oversees the biophysical MBioFaSt platform of

the laboratory which contains many instruments useful to all teams within the Unit and (2) the team has many collaborations as highlighted in the HCERES presentations. Over the period of evaluation, they contributed to 40% of the shared publications with 6 teams (E03, E04, E09, E10, E11, E12) of the unit and ongoing collaborations existed with other teams (E04, E05). The director of the unit presents each year all the facilities to the new incomers to promote more collaborations between the teams.


4- *“The committee advises the team to take advantages of their current network of collaborations to investigate the possibilities of obtaining more important national and international fundings.”* The team has always been able to obtain key financial support at the national and European levels, which highlights its attractiveness, including industrial partners.

Team E05. Pathogenesis of bacterial infections and immunity

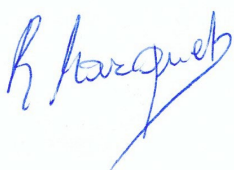
“The main weakness of the team is its small size. Another potential weakness is the absence of interactions with other groups from the unit or the institute”. At the beginning of 2019, the team started with 3 PhD students and 1 M2. Very quickly the team recruited a postdoc in 2020, and later a CNRS assistant engineer arrived in 2021. As mentioned in the auto-evaluation report, the team brings to the Unit its expertise in developing models for infectious diseases caused by bacteria, and on the other hand the expertise of the unit will favor projects linked to RNA machineries in bacterial infections. In addition, the team has been joined recently by an assistant professor (March 2022) who brings his expertise in RNA biology to monitor the RNA transcriptome of cells infected by *Shigella* and its virulence effectors. Because the team is focusing on oxidative stress and the role of oxygen depletion caused by bacteria infection, it has developed new tools and strong interactions have already been established with at least four teams (E03, E04, E07, and E09). Therefore, the team has rapidly evolved in two years and its integration within the unit is already successful.

Team E08. Non coding RNAs and viral infections

“The team currently lacks a long-term funding support”. Besides ANR project, the team with its topic is one of the founders of the first LabEx NetRNA (2011-2021) and is now partner of the ITI IMCBio+ (2021-2028) which comprises the LabEx NetRNA and the graduate school IMCBio (2018-2028).



Dr Pascale Romby
Director UPR 9002 CNRS



Dr Roland Marquet
Deputy Director UPR 9002 CNRS

I
Monsieur Éric Saint-Aman
Directeur du Département d'évaluation de la recherche
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Strasbourg, le 11 avril 2023

Objet: Rapport d'évaluation DER-PUR230022968 -ARN -Architecture et réactivité de l'ARN

Réf.: RB/FF/ 2023-209

Rémi Barillon

Vice-Président Recherche,
Formation Doctorale et Science
Ouverte

cher Collègue,

Nous vous remercions ainsi que tous les membres du comité HCERES pour le travail d'expertise réalisé sur l'unité de recherche « Architecture et réactivité de l'ARN » (ARN-UPR 9002).

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La tutelle CNRS a indiqué qu'elle n'émettrait aucune observation de portée générale suite au rapport d'évaluation transmis.

Je vous prie d'agréer, Cher Collègue, l'expression de nos cordiales salutations.

Rémi Barillon

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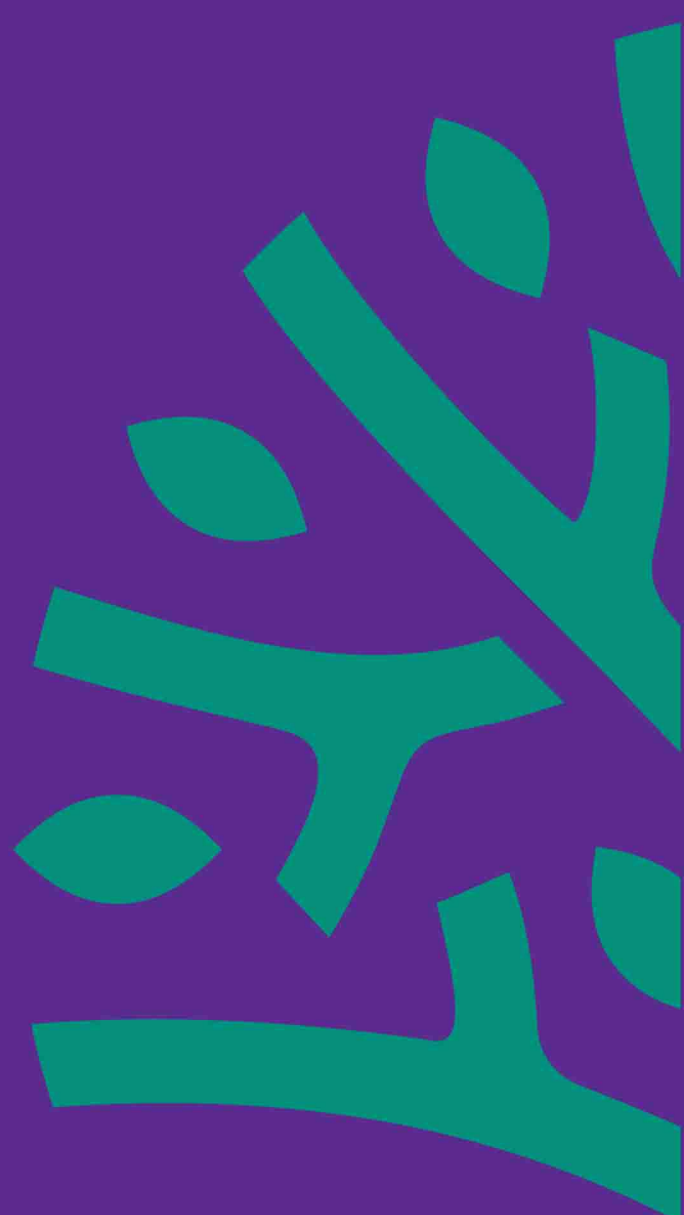
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