Research evaluation

EVALUATION REPORT OF THE UNIT

Ingénierie Moléculaire et Physiopathologie Articulaire

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Université de Lorraine
CNRS

EVALUATION CAMPAIGN 2022–2023
GROUP C

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High Council for evaluation of research and higher education

In the name of the expert committee[1]:

Isabelle LANDRIEU, Chairman/Chairwoman of the committee

For the Hcéres [2]:

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:	Mrs Isabelle Landrieu, CNRS, Villeneuve-d'Ascq
	Mr Philippe Huber, CEA, Grenoble
	Mrs Catherine Moali, CNRS, Lyon
Experts :	Mr Renaud Vincentelli, CNRS, Marseille
	Mr Lucas Jacques Waltzer, CNRS, Clermont-Ferrand
	Mr Christophe Egles, UTC, Compiègne

HCÉRES REPRESENTATIVE

Mrs Marie-José Stasia

CHARACTERISATION OF THE UNIT

- Name: Ingénierie Moléculaire et Physiopathologie Articulaire
- Acronym: IMoPA
- Label and number: UMR 7365
- Number of teams: 6
- Composition of the executive team: Jean-Yves Jouzeau (Director), Bruno Charpentier (Deputy-director)

SCIENTIFIC PANELS OF THE UNIT

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

SVE6 : Physiologie et physiopathologie humaine, vieillissement

SVE4, SVE7

THEMES OF THE UNIT

The Molecular Engineering and Articular Pathophysiology unit (IMoPA) develops research ranging from deciphering the molecular mechanisms of RNP assembly and RNA processing (Team 1), of glycosyltransferases function and glycosamino glycans assembly (Team 2) and of polyketide synthesis by mega-enzymes and regulation by cysteine-containing enzymes (Team 3), to bioengineering: to remodel and control joint inflammation (Team 4), to produce multilayered biomaterials functionalised with cells differentiated from mesenchymal stem cells MSCs (Team 5) and to make clinical use of the immunomodulatory properties of MSCs or specific immune cell populations (Team 6).

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

IMoPA (UMR7365 CNRS-University of Lorraine) was created in January 2013 by the fusion of UMR 7214 AREMS (RNA, RiboNucleoProteins structure-function-maturation, Molecular and Structural Enzymology, located on the Faculty of Sciences & Technologies campus) and UMR 7561 PPIA (Articular Pathophysiology, Pharmacology and Engineering, located on the Medicine campus). It is now located on the 'Campus Brabois-santé', following the move of both initial units in the newly built 'Biopôle de l'Université de Lorraine', in the frame of the 'plan campus'. IMoPA is now in the same building as most of the core platform facilities provided by UMS2008 CNRS-US40 INSERM-UL IBSLor (Engineering in Biology & Health Lorraine) and near the central animal housing facilities of the University. From the five original teams (2013–2016), one additional, now Team 6, was created for the last contract (2016–2021).

RESEARCH ENVIRONMENT OF THE UNIT

IMoPA is a joined research unit between the University of Lorraine (UL) and the National Center for Scientific Research (CNRS). It belongs to the scientific pole Biology, Medicine & Health (BMS) of UL. IMoPA unit is involved in the 'Lorraine Université d'Excellence' (LUE) I-SITE initiative that has been granted in 2016 in the frame of PIA2 and has been renewed in June 2021. The contribution of IMoPA to the steering of this excellence initiative has been through the impact programmes Biomolecules dedicated to the valorisation of natural extracts and Geenage dedicated to normal and pathological ageing, both co-headed by an IMoPA member. IMoPA is one of the founding members of the service unit IBSLor that was launched in January 2018. The IBSLor director, a coordinator of its steering committee, three heads out of the six platforms, and several persons in charge of various IBSLor equipment are IMoPA members. Five poles from the platform have received the label of StAR (Structure d'appui à la Recherche) within the I-Site programme LUE INFRA+ and two have IBISA labels (including the EpiRNA-Seq pole managed by an IMoPA team). Several IMoPA teams are in close collaboration with the clinical departments of Nancy university hospital, and IMoPA hosts several teacher researchers with hospital duties. They participate to the translational excellence initiative FHU Cure of the region Grand-Est (related to chronic inflammatory diseases) and FHU Cartage (to find biomarkers of heart failure). IMoPA has been involved in the State Region Contract Plan (CPER) for Lorraine 'Technological Innovations, Modelling and Personalised Medicine' (IT-M2P) from 2015 to 2020 and in the Region Grand-Est CPER 2021–2027 'Grand-Est Institute of Inflammation' (I2GE) and 'Grand-Est Medicines' (GE-MED).

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

Permanent personnel in active employment	
Professors and associate professors	17
Lecturer and associate lecturer	23
Senior scientist (Directeur de recherche, DR) and associate	6
Scientist (Chargé de recherche, CR) and associate	7
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	28
Subtotal permanent personnel in active employment	**81**
Non-permanent teacher researchers, researchers and associates	6
Non-permanent research supporting personnel (PAR)	5
Post-docs	6
PhD Students	27
Subtotal non-permanent personnel	44
Total	**125**

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

Employer	**EC**	**C**	**PAR**
Université de Lorraine	40	0	17
CNRS	0	10	11
Inserm	0	3	0
CHRU Nancy	0	0	0
Others			
Total	**40**	**13**	**28**

UNIT BUDGET

Recurrent budget excluding wage bill allocated by parent institutions (total over 6 years)	**1627**
Own resources obtained from regional calls for projects (total over 6 years of sums obtained from AAP idex, i-site, CPER, territorial authorities, etc.)	4467
Own resources obtained from national calls for projects (total over 6 years of sums obtained on AAP ONR, PIA, ANR, FRM, INCa, etc.)	3225
Own resources obtained from international call for projects (total over 6 years of sums obtained)	1265
Own resources issued from the valorisation, transfer and industrial collaboration (total over 6 years of sums obtained through contracts, patents, service activities, services, etc.)	1591
Total in euros (in K€)	**12175**

GLOBAL ASSESSMENT

The research unit IMoPA combines complementary approaches from the molecular enzymatic and structural levels to cellular engineering and biomaterial design, creating strong opportunities for interdisciplinary approaches. Institutional support is excellent, with the recruitment of three teacher researchers (MCF UL), one full-time researcher (DR CNRS) and seven research support persons. Supervision activities have been excellent with 63 Master 2 internships, 48 PhD defences, 28 ongoing PhDs, 28 postdoctoral fellows and multiple additional undergraduate internships. IMoPA benefits from very good equipment to conduct its research structured in the mixed service unit Engineering, Biology, Health in Lorraine (UMS2008/US40 IBSLor) providing state-of-the-art technological equipment and unique know-how.
IMoPA has shown a very good scientific output, with international visibility in every team. The unit published 230 articles, some in journals of high-visibility (Angew Chem, JACS, Mol Cell, Nature, Nat Comm, NCB, NAR, PNAS, Annals of rheumatic diseases, Leukaemia…) and some in more specialised well-regarded journals (J Mol Biol, Human Mut, RNA, Structure, Faseb Journal), with 41 resulting from collaborative projects. Some original research lines are competitive at the international level, including research on post-transcriptional modifications of RNA molecules, on mega-enzymes that catalyse complex natural compounds, on redox chaperones, on biosynthesis of GAGs by glycosyl transferases, or on the link between osteoarthritis and bowel inflammation diseases. These research lines have a significant impact on the biomedical or bioengineering field. Research lines related to bioengineering of cells or biomaterial design are excellent and present unique translational opportunities based on high-end methodologies. Focus on these strengths is essential.

The funding level has been excellent and IMoPA has taken full advantage of all the opportunities including at the national level with eighteen projects from ANR, one from INCA, one from ANRS and five from FRM, complemented by 45 projects funded by charities and patient associations. In the context of the PIA, IMoPA benefited from I-site LUE (Lorraine Université d'Excellence) initiatives with 22 funded projects and from the pôle Biologie, Médecine, Santé (BMS) with seventeen funded projects. At the international level, four collaborative projects have been funded by ANR PRCI, one in the context of interreg and one was obtained from Eurostar. The European project Psoriacure is a joined effort between academic labs and companies to find a new treatment for psoriasis. Although very good, the participation to international collaborative networks could be increased.

IMoPA has shown during the last period an outstanding valorisation activity, including the creation of a spin-off company named Steminov to develop the therapeutic use of stem cells in septic choc treatment and of the Labcom Anthralab with Abolis Biotechnologies in Evry in the biotechnology field (biosynthesis of dyes). Both these initiatives directly emerge from IMoPA original scientific expertise. Altogether, eleven patents have been published, four of them with inventors from two distinct teams. A sizeable part of the unit budget, not including salaries (30%) have originated from eight maturation projects provided by SATT Sayens for a total amount of 1,576 K€. Two units' members co-directed the technology network IMPACT from I-site LUE (Biomolecules and GEENAGE) that promote the interactions with industrial partners. Translational activity is excellent, with 21 clinical trials and 160 clinical articles during the period involving IMoPA clinicians and supported by close contact of team 6 with the university hospital of Nancy.

IMoPA had excellent interactions with patient associations (Alzheimer, associations Espoir et Capucine, FRM, Maladies rares…), including funding of its research projects for a total amount on the period of 1,688 K€. Interesting efforts have been made to reach the general public, including through press releases, an apple podcast and radio and TV interviews, now available on YouTube. Teams 5 and 6 have been active in participating to various animations and very well exploited their proximity to the clinic to reach the public, contributing to education and preventive actions and to provide nine technico-or medico-legal reports to control authorities (e.g. ANSM).

DETAILED EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The internal collaborations have increased as shown by the 41 original articles, eight international reviews and two patents that are co-authored by members of different IMoPA teams. However, these interactions are mainly driven by team 5 and more specifically team 5 with team 4 or 6, showing some remanence of the historical structure. International funding has been obtained, to support mobility and networking (2 COST actions, three PHC, 1 GDRI -1 LIA) or research collaborations (2PRCI, 1 eurostar, 1 EU joint programmes on rare diseases) with an additional FEDER support and one Interreg. No specific action has been taken by the Unit to facilitate access to challenging EU programme, including internal funding to support mobility. However, a 'correspondant international' has recently been appointed who might improve access to optimal information about opportunities suited to the Unit profile.
The translational and valorisation potential of the Unit has been very well exploited, mainly stemming from the teams' own initiatives and strong support from the SATT Sayens. Communication to the public has been modest at the Unit level but this point must be mitigated by the sanitary emergency conditions that have impacted many opportunities.
Involvement in training is excellent with 48 PhD defences, and 63 Master students supervised within IMoPA. In addition, 28 postdocs have joined IMoPA but sometimes for very short duration (I year or less). International attractiveness among these young researchers remains low but nevertheless improved compared to the previous period (7 PhD students and 5 Postdoctoral researchers). Improvement of the IMoPA steering organisation and resource allocation is still underway and reorganisation has not yet been fully achieved.

B – EVALUATION AREAS

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

Assessment on the unit's resources

IMoPA takes excellent advantage of all the programmes available, at the regional and national levels, to allow its research programme to proceed. Recruitment has largely compensated the external mobilities and brought new expertise to the Unit. However, these recruitments do not seem to have been used as an instrument of the common scientific strategy. Internal mobility and sharing of workforce resources are too limited. The infrastructures are very good and suited to the research programme. Maintenance, repair and renewal of IMoPA equipment is, however, a strong budget concern despite major efforts to safeguard the technical assets within the IBSLor platform.

Assessment on the scientific objectives of the unit

IMoPA teams have developed know-how and knowledge that provide an international visibility to some timely and original topics of research. Two major strategic lines defined by IMoPA concern exploitation of results and translational research. Risk of dispersion is important at several levels: inside the teams that mostly present multiple parallel axes or research lines, at the level of the Unit that has difficulties to maintain a clear scientific perimeter and at the level of the activity profile with the need to balance increased exploitation and translation, expected by supervisory bodies, with the current excellence of the basic research.

Assessment on the functioning of the unit

The Unit complies with the multiple organisational institutional requirements of an UMR to ensure the well-being and security of its staff. Recognition of all the individual contributions seems to be excellent as attested by the promotion received by its staff and the inclusion of all staff professional categories in the publication authorship. The inter-team interactions are good and attested by co-authored publications and shared interns and PhD students. In a manner that is not specific to IMoPA, costs of equipment acquisition, maintenance and renewal is very high. However, given the very large field of expertise of IMoPA, the teams have a broad range of technical needs that amplifies the concern. The internal funding policy of sharing a large part of the institutional support with the teams, according to workforce, deprives the Unit of much of its strategic capacities. The decision-making chain at the Unit level is not clearly defined.

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

Strengths and possibilities linked to the context

The Unit has benefited from a very good institutional support in terms of human resources with six recruitment/incoming mobility of researchers (1 DR2 CNRS, 3 MCU and 2 MCU-PH of UL) and seven of ITA (5 UL and 2 CNRS) compensating respectively ten (including 5 retirements) and four (including 1 retirement) outgoing mobility. IMoPA makes excellent use of the local support of SATT Sayens (7 pre-maturation and 7 maturation projects) and the Biomolecules and Geenage impact programmes of the I-Site LUE initiative. It has multiple interactions with the university hospital-CHU and received support from CPER projects (IT-M2P, I2GE, GE-MED). Funding by competitive grants has shown a considerable increase compared to the previous contract, with a ratio reaching almost five when comparing 2016 with 2021. Recurring funds have in the meanwhile decreased in volume (-10%) and proportion (from 31% in 2016 to 8% in 2021).
IMoPA has a balanced composition with one third of the permanent researchers being full-time researchers and one third of all research members being supporting staff. Non-permanent IMoPA members, including PhD students represent one third of the total workforce.
The inter-team interactions attested by 41 co-authored original publications and shared interns and PhD students is in progress compared to the previous contract.

Weaknesses and risks linked to the context

A large part of the institutional resources of the unit (65%) is distributed between the teams, weakening the capacity of the direction to invest in shared actions and support maintenance, repair or equipment renewal of general interest. In addition, given the diversity of expertise, a high level of diverse equipment is needed, with probably a low level of shared use between teams for some of them.
Staff support is imbalanced between teams and a general strategy to use the available expertise in a more rational manner, although considered, is not in place. Recruitment and incoming mobility do not follow a clear scientific strategy.
The expansion capacity to offer working space for new teams (emerging or incoming) is limited within the building.
IMoPA benefits from a leader position in Biology and Health within UL campus but concomitantly suffers from a weak critical mass of researchers in the field.

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

Strengths and possibilities linked to the context

IMoPA has an excellent expertise in a number of original topics with international visibility: RNA post-transcriptional modifications, mechanistic investigation of the link between bowel and joint inflammation, osteopathies, rare diseases linked to glycosyltranferase mutations, megaenzymes in polyketide synthesis.
The unit has an excellent interdisciplinary potential, with expertise ranging from molecular to cellular aspects, scaling from bench to bedside and covering protein, sugars and nucleic acid knowledge and know-how.
The fundamental research conducted in the unit is relevant to biomedical applications, covering rare diseases (Prader-Willi syndrome, Ehlers-Danlos syndrome) or chronic diseases linked to cancer and inflammation. The basic research supports the identification of biomarkers for personalised medicine (identification of patients with

IBD at risk for arthropathy based on microbia signature) and new targets for intervention by deciphering molecular mechanisms and pathways (regulation of genes by GAGs or long non-coding RNA). The translational research conducted in the Unit provides new and cutting-edge intervention options based on cell engineering (e.g. iNKT cells) or regenerative medicine (e.g. 3D bioprinting material). Finally, new therapeutic compounds are evaluated and their biotechnological production explored (e.g. engineering of polyketide enzymes).
Two major strategic lines were identified and validated:

1) to amplify translational research based on clinical contacts
2) to improve the transfer & valorisation.

Weaknesses and risks linked to the context

The multiplication of the research lines, with several teams conducting two or three axes of research led by PIs, is a risk of dispersion of the resources and loss of international recognition. As noted in the auto-evaluation report, the clinical field of investigation has also been enlarged and now encompassed gastroenterology, haematology and oncology in addition to the historical and recognised rheumatology field. To maintain the clinical interactions and translational activity on such a broad field is challenging.
IMoPA steering committee has mainly a bottom-up approach concerning the general scientific strategy of the Unit and inter-team interactions and resource sharing. Incentive support for international actions was not committed. The frequency of the meetings between team leaders has been low and focused on practical discussions. The balance between team identity and the unit common visibility is low.

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

IMoPA has an excellent parity on the general level that is also respected in the laboratory council (50/50) and among the team leaders (50/50). Procedures are in place for the incoming staff based on NEO and prevention documents. Six persons are covering hygiene and security of IMoPA supported by five radiation advisers (one for X-rays). A specific technical training on equipment is provided for the newcomers. Magnetic card access and alarm systems ensure security of the building while restricted areas within the building allow limiting access to sensitive products or equipment. The disposal of waste and the periodic control of sensitive equipment (e.g. autoclave) comply to the supervisory authorities regulation. A specific procedure for temporarily isolated personal is detailed. Concerning the IT security, the Lorraine University provides an excellent management support though its IT service that is likely to minimise the risks. Scientific data storage capacity is good and back-up plans implemented. A training plan is edited and validated every year.
The COVID lockdown was well managed by the direction team, based on a continuity plan that was elaborated in emergency conditions. The laboratory has shown resilience. The unit is taking all measures within its previews to limit its environmental impact (e.g. encourage cycling to the lab by installing showers and contribute to tree plantations).

Weaknesses and risks linked to the context

Efforts to prevent psychosocial risks are not formalised. A survey of students and ITA were conducted but no working group was active (yet) to analyse the results and take the potentially needed actions. No survey directed at the researchers was conducted, neither before nor after the sanitary crisis. The 'Règlement intérieur' needs to be updated to comply with supervisory requests (CNRS template). An institutional involvement is needed to go further in reducing the carbon footprint because it is linked to the existing infrastructure.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

IMoPA teams have been very active and successful at funding their research, attesting its quality given the level of competition. Visibility is excellent at the national level, with participation to learned societies and institutional scientific committees. IMoPA members have contributed to the editorial process by participating to editorial boards and special issues and to international conferences, both as organisers in a number of instances, or as invited speakers. IMoPA members have made additional contributions to international visibility by participating to networking projects at the international level. Incoming international mobility remains however low. Funding schemes within the horizon Europe frame could be more exploited given IMoPA research, education and innovation assets, particularly in Human Health.

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

International student exchange and networking were promoted by three PHC, and members of IMoPA integrated the management structure of two COST actions EuroSoftCalcNet and Epitran. Members of IMoPA participated to the organisation of twelve international conferences, including two in Nancy and two in the frame of the GDRI France-Chine.
Members of IMoPA are elected members of national learned scientific societies (SFBBM, SFBTM, toxicology, SoFCOT, SFMCP, SFHG, SFGM-TC, SFBCT) or one international society (RSC UK). They have received four prizes for the best communication in national congresses and four times the Wittner prize from the Medecine Faculty. Two emeritus members were promoted officer and commander of the Légion d'honneur respectively, for their contribution to research steering. IMoPA members participated to edition, as guest editors, of six special issues and one member is editor in chief of a book series (RSC, UK, Chemical Biology).
IMoPA contributes to the steering of the supervising bodies by participating as invited or elected members of CNRS committee section 28 and Universities CNU64.
The website of the Unit is informative and was upgraded.

Weaknesses and risks linked to the context

Invitations to international congresses are limited to a small number of very active members with excellent visibility.
The number of international students and postdocs attracted to join IMoPA is low: Only five postdoctoral fellows (among 28) and seven PhD were on international mobility. Only eleven postdoctoral fellows stayed in the lab beyond one year.
Participation to editorial boards of well-recognised journals is limited.
Part of the website information would benefit from an English version by increasing the international visibility.
Invitation to give laboratory-wide seminar events are irregular and rely on the master invitations. More targeted invitations would strengthen IMoPA national and international networks and benefit the laboratory.

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

Strengths and possibilities linked to the context

IMoPA has a very good attractiveness at the local level of the University for PhD training (48 PhD defences and 28 ongoing PhD) and hosted multiple additional internships (including 63 Master 2).
The number of CR to DR and MCU to PU promoted during the contract is very good, with five "changements de grade" et five "changements de corps". Promotion of the supporting staff is excellent with thirteen ITA promoted during the contract: five "changement de corps", eight "changement de grade" (among 27 ITA), so that 50% of the supporting staff was rewarded for its involvement, showing a strong and efficient support of the applications and recognition of the individual involvement in the unit operations. University degrees for two ITA in parallel of their job (PhD) were supported.
One CNRS DR2 on international mobility was recruited. three MCU and two MCU-PH have joined the laboratory. Four research supports members (3T and 1 AJT from UL) have joined IMoPA teams based on internal or external recruitment. In addition, one administrative support staff was obtained for the collective service as well as two positions for the mouse housing facilities (1 AI CNRS and 1 AJT UL).

Weaknesses and risks linked to the context

No formal, unit-wide, process to attract young researchers with potential to apply to full-time researcher positions at EPST (CNRS, INSERM…) is in place.
The person in charge of glass ware management has left the laboratory and has not been replaced. Consequently, this very important task needs to be managed by the research support staff in a collective manner that is not easy to organise and might be the source of frictions.
Internal and external laboratory-wide seminars are not organized on a regular basis. The only seminar room is too small to welcome all IMoPA research workforce. Early-stage researchers, Masters, PhDs and Post-docs have no internal networking activities.

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

IMoPA team's collectively received funding for International projects with two ANR PRCI with Germany and one with Switzerland. Team members joined two European networks: joint programmes on rare diseases PHYSPATH-KS and Psoriacure (Eurostars) and participated to one Interreg IMPROVE-STEM.
A 'Groupe De Recherche International' France-China supported by the CNRS has been created since 2016 with Wuhan University in the field of Regenerative Medicine that has evolved towards an International Research Network (IRN) from 2021.
A 'correspondant CNRS' Europe has been nominated to ensure internal information about the ongoing calls and the organized webinars.
IMoPA showed a very good capacity to join national networks, thanks to its original expertise and methodologies, as well as the relevance of its scientific goals. The general funding part from competitive ANR AAP is in steep increase compared to the previous contract, with 22 selected projects (all actions), including a good proportion (7) as coordinators. One INCA grant has also been received, as coordinator of the project and one from the ANRS.
IMoPA makes excellent use of the local/regional opportunities for funding of a PhD. Support is obtained at the local University level from the scientific pole BMS for equipment repair/renewal and from the CHRU for interface contract (postdoc funding) and translational research, as well as FEDER funding through the region grand-Est (2 programmes involved). (Co-) Funding for PhD has been obtained, including by the PIA ISite LUE and the region Grand-Est.

Weaknesses and risks linked to the context

The number of European research projects is low in regard to IMoPA research originality and quality and its resources.
The proportion of ANR proposals submitted as coordinators could be increased to further support IMoPA strategic research plans.

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

Strengths and possibilities linked to the context

IMoPA benefits from excellent technical infrastructure for multiple methods from biophysical techniques (NMR spectrometers, X-ray diffractometer) to cell analysis (flow cytometry) and animal assays, as well as bioprinting. IMoPA has additionally access to IBSlor and the animal core facilities of the university. The unit is conveniently located next to the IBSLor UMS and animal facilities. I MoPA members have contributed to the structuration of their equipment into the six poles of the platform IBSLor and they have an excellent involvement in the platform operation and scientific expertise. Two members of IMoPA are respectively Director and coordinator of the platform. Epi-RNA-Seq (new) and PTIBC (imaging, renewed) received an IBISA labelisation. Other poles are engaged in a quality label process at the local level of the University.
Multiple and original skills are found in the unit including, but not limited to, characterisation of glycans, characterisation of RNA splicing and post-transcriptional modifications, cell reprogramming, bioprinting, protein engineering, single-cell transcriptomics.

Weaknesses and risks linked to the context

The absence of a regional facility for cryo-EM needs to be compensated by external collaborations.
The capacity to renew or upgrade large equipment (e.g. a cryo-probe) is impinged by the scarcity and lack of (time) flexibility of funding opportunities devoted to these types of actions.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The overall production of IMoPA is excellent with some contributions being outstanding. All the members of the Unit are associated with the publications. Nevertheless, publications of junior members are proportionally too low (in quality and/or quantity), or too slow, in regard to the high-standard expected to pursue research careers. High-profile publications with excellent visibility have been produced but with some heterogeneity in the distribution of the total production between the teams. Proportion of open-access manuscripts is very good but systematic deposition of data is not yet practised. Data management and protection are excellent, with an internal document sharing system and back-up solutions and storage capacities. Regulation concerning ethical concerns are followed, and information is provided to raise the awareness of unit members regarding research integrity.

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

Strengths and possibilities linked to the context

The Unit members published exclusively in scientific peer-reviewed journals. The Unit has collectively published 237 original articles for a research resource equivalent of 33 persons, which corresponds to about seven articles per researcher during the last period or 1.5 per year. 102 of these articles were published with an IMoPA member as first, last or corresponding author. 47 of these original articles can be considered of high visibility at the international level. This original research production is complemented by 64 review articles including ten reviews with an excellent contribution to the field. 181 clinical articles have been produced, with eleven of them with excellent impact in the field. The clinical articles are originating from teams 1 and 4 to 6. Research conducted by IMoPA teams is original and of quality. High-profile research results of broad scientific interest were published in very reputed international scientific journals such as Angew Chem, JACS, Mol Cell, Nature, Nat Comm, NCB, NAR, PNAS, Annals of rheumatic diseases, Leukaemia … and more specialised results in well-regarded journals such as J Mol Biol, Human Mut, RNA, Structure, Faseb Journal, oncogene, Cell death and differentiation.
Team 1 has improved knowledge on the biogenesis of eukaryotic box C/D small nucleolar ribonucleoproteins by revealing molecular detail of the interaction of Bcd1p, that participates to its co-transcriptional initiation, and Rtt106p a histone chaperone (published in Nat Com 2021). Team 3 has contributed to the very original characterisation of a monoamine oxydase that displays a dual enzymatic activity to form a polyketide macrocycle (Nat Commun. 2018) with impact in synthetic biology as a potential general cyclisation enzymatic tool. The redox group uses its high expertise in redox biochemistry to decipher a complex pathway involving the scaffold protein Ybp1 that chaperones a cysteine to sulfenic acid oxydation in H_2O_2-inducible transcriptional response in yeast (published in Nat Chem Biol 2018). Team 4 provided important results regarding the role of PPAR-gamma in the activation of type 2 Innate Lymphoid Cells (ILC2s) in acute airway inflammation (Mucosal Immunol 2021). They also characterised the first animal model of osteoarthritis induced by a metabolic syndrome, and showed that the administration of eplerenone, to reduce metabolic alterations, decreases joint degeneration (Ann Rheum Dis 2018). Team 6 has also identified the very interesting prognostic and therapeutic potential of a subset of immune cells in the context of allogeneic haematopoietic stem cell transplantation (CD4- iNKT, Leukaemia 2016 and Oncoimmunology 2018). The development of virus-specific T cells (VSTs) to treat viral infections has also been nicely exploited in several clinical trials (J. Hematol Oncol 2017).

Weaknesses and risks linked to the context

As mentioned before, the IMoPA unit succeeds in developing a multi-scale and multifaceted bioengineering research with a range of specific focus. However, the excellent basic research conducted in this unit should remain the cornerstone of its activity profile. Thus, it will be delicate but not impossible to make these two types of research coexist at equal strength.

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

All the staff is associated to the publications of the Unit. All the individual contributions seem to be properly taken into account (involvement of students, ITA, junior members).

Weaknesses and risks linked to the context

The teams have a non-homogenous impact concerning publications in reputed international journals.
28 postdoctoral fellows have been hosted with a majority for too short-term stays to be productive.
Research communication by the PhD students and post-doc is on average relatively (to the high standard expected for a career in science) low in quantity and/or quality, or delayed.
(Some) teacher researchers at the MCU level seem to have difficulties to develop their own project, given that their authorship contribution is mainly as co-authors rather than responsible authors.

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

An internal data sharing e-space (EscoLa) and use of Lab notebook both facilitate analysis of the raw data.
Staff members are well informed of the recommendation for scientific integrity by sending documents via mailing lists. PhD students followed a mandatory module on research integrity provided by the doctoral school.
An authorship policy is implemented and formally included in the 'règlement intérieur'.
Excellent efforts have been made to provide open access to the published manuscripts using deposition in HAL repository. Data are deposited in well-established databases PDB or BMRB.
The interactions with patient associations, at the level of funding or participation to scientific or administrative councils, facilitates the inclusion of patient concerns into the research goals.
Regulatory rules concerning animal handling, informed consent for human-based material and patient inclusions are followed. Protocols are submitted to ethical committee at the local or national level. Infrastructures are accredited and experimenters followed specific training and accreditation according to their level, including renewal on a periodic basis.

Weaknesses and risks linked to the context

The unit has not switched yet to electronic lab book. It does not seem that measures are in place at the unit level to limit the use of animal experiments.
Publication of full datasets associated with publication and pre-print publication, when relevant, do not seem to be a regular practice (at the notable exception of team 1). IMoPA workforce is well gender-balanced (54% female/46% male as a whole and 51% female/49% male for research teams). However, imbalances observed are a female minority for researchers/teacher researchers (43%) and a majority for scientific supporting staff (73%).

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

IMoPA has made consequent efforts to contribute to society through its scientific expertise and basic research by exploiting its results to provide innovative products relevant to health improvement and the bioeconomy. Members of IMoPA sustain contact with patient associations and multiple projects were funded by charities, showing the interest raised by their proposals. The members of the Unit closer to the clinical field have participated to patient education and provided recommendations. Some actions have been taken to reach the younger public, but it could be improved. IMoPA has taken some steps towards open science but is not yet fully committed to this new practice of science.

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

Strengths and possibilities linked to the context

The translational potential of the teams' research expertise has been very well exploited, with support from the SATT Sayens, resulting in the filing of eleven patents with six international expansions and one licensed patent.
One start-up Steminov was launched during the contract based on the strong asset in stem-cell production available in the unit, with a therapeutic goal against sepsis. A unique and well-recognised cell therapy unit

(UTCT) which is involved in clinical trials both at the national and European levels has been established by Unit members.
One Labcom (Anthralab) with Abolis Biotechnologies was set up, involving two full-time Abolis company staff. Nine R & D contracts with companies were concluded. Support from SATT Sayens amounted through seven pre-maturation and seven maturation projects to a total of 1,576 K€. Two units' members co-directed the technology network IMPACT from ISite LUE (Biomolecules and GEENAGE) that promote the interactions with industrial partners. The European project Psoriacure is a joined effort between academic labs and companies to find a new treatment for psoriasis.
IMoPA has excellent involvement with patient associations, attested by the excellent support of diverse charities, with about 45 research projects supported by foundations Alzheimer, ARTHRITIS COURTIN, de l'Avenir associations Espoir, Capucine, Kayak de l'espoir, Laurette Fugain Vaincre la mucovisidose, Fédération Leucémie Espoir, Union Nationale des Syndromes d'Ehlers-Danlos Ligue contre le cancer (21), FRM, Fondation Maladies Rares, arthritis-Courtin that collectively contributed for 1,688 K€.
Four members are invited to participate to the scientific committee of charities and one to the administrative council.
Nine technico or medico-legal reports have been provided to the ministry of justice, ANSM or other control authorities and two recommendation reports have been published in professional journals.
The biomolecule impact initiative provides a leaflet to companies concerning the expertise of the participating academic laboratories. Two of the international conferences organised within the Biomolecule impact programmes gathered industrial partners and round tables focused on bioeconomy.
Technical expertise and know-how are also provided to industrial partners through the IBSLor platform.

Weaknesses and risks linked to the context

Communication at the unit level of IMoPA research and technology to potential industrial partners is not in place.
There is no systematic approach to sustain the valorisation effort, which is dependent on SATT Sayens financial support.
They were no PhD (co-) funded by companies, such as within the programmes CIFRE.

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

Strengths and possibilities linked to the context

IMoPA is involved in research area with a strong impact on Human Health and conduct research from the mechanistic molecular aspects of diseases to the clinical trials, with impact ranging from long-term to optimisation of existing treatments.
Besides Health, some innovations emerging from IMoPA research and relevant to biotechnology and bioeconomy are of interest, e.g. elimination of wine sulphites or production of dyes (anthralab).
The innovative potential of the IMoPA teams is attested by its successful application to i-Lab BPI France competition for start-up launch in innovative technologies (2019).

Weaknesses and risks linked to the context

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

Strengths and possibilities linked to the context

Interesting efforts have been made to reach the general public, including through press releases, an apple podcast and radio and TV interviews, now available on YouTube. Teams 5 and 6 have been active in participating to various animations and very well exploited their proximity to the clinic to reach the public, contributing to education and preventive actions.
Punctual but encouraging initiatives have been taken to reach pupils (an experiment demonstration) and college students (internship during vocational days).

Weaknesses and risks linked to the context

The dissemination of knowledge to the general public remains low and is not an effort shared by all teams

C – RECOMMENDATIONS TO THE UNIT

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

The excellent basic research conducted by IMoPA is and should remain the cornerstone of its activity profile. The Unit should strive to define clear strategic priorities and commit resources according to these priorities. This might require to consider maintaining a Unit budget sufficient to support its policy. Given that the teams have been very successful in funding their research, a larger share of the budget, from the institutional support and/or by levying some charges on the teams' contracts, could be devoted to strategic actions. One example would be to support the challenging task of submitting proposals at the European level, by funding writing support or networking travels.
Regular meetings of the team leaders seem a necessity to define the strategic objectives and policy of the Unit. The set-up of this supervisory board would be facilitated by a prior definition of the Unit's teams' contour and their representation by a group leader. This supervisory board would be, together with the direction committee, responsible for the allocation of the common resources. These resources should not be considered as historical inheritance, but rather as instruments of the Unit strategic priorities, to the benefit of all researchers. As such, research support of the ITA workforce should be allocated to provide the broadest benefit. The Unit should set in place a common process to attract and support candidates with the potential to integrate research bodies as full-time researchers, to complement the Unit expertise in areas commonly defined as priorities. The Unit should also define clear channels of discussion and decision, both at the unit and local level, to favour the common use of equipment and its rational operation.

Recommendations regarding the Evaluation Area 2: Attractiveness

International visibility should be further extended by the broader participation of team members, including PhD students and post-doc, to international meetings. Some of the website pages could be translated into English to be accessible to the international community. The unit should pursue its global efforts of international networking and mobility. Regular unit-wide internal and external seminars need to be organised that could take the form of a hybrid gathering given the limited size of the auditorium (nevertheless well equipped with video conference facilities). This could include more frequent invitations of external researchers to give seminars to the whole Unit, opening up new opportunities for networking. Early stage researchers should be given the opportunity to present at this seminar series as part of their training in communication to a diverse audience. The early-stage researchers should take the initiative of internal Unit-wide networking activities (e.g. annual meeting of the incoming master students) and should provide their savviness in social media to improve visibility of their work within the laboratory. Participation to Horizon Europe calls should be encouraged given that IMoPA field(s) of expertise, and valorisation actions, closely match the programme interests in the Health cluster, more specifically mission cancer, and the innovation pillar. Advantage should be taken of the institutional support to build and write these challenging EU proposals. Efforts that were initiated to acquire a cryo-EM microscope that could be used at the regional level and could be at least sufficient to make the initial quality screens of the grids should be pursued.

Recommendations regarding Evaluation Area 3: Scientific Production

Efforts should be pursued to publish research highlights in high-profile and well-esteemed journals. This goal could be best achieved by strengthening the internal multidisciplinary interactions and by increasing participation in international collaborative networks. Attention should be paid to maximise the timely scientific production of the PhD students and Post-doctoral fellows to strengthen their career opportunities. The researchers that do not benefit from a full time to develop their projects should be offered support, which could take the form of funding or technical help, to be able to take more prominent roles in projects and publications.

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

Open sciences practice should be strengthened by increasing data sharing, using preprints and repositories for raw or process data. Communication to the public should be increased in view of promoting health literacy to increase informed health decision-making and to attract young students to a career in sciences. Unit members should also take advantage of their interactions with patient associations to incorporate research lines considered as priorities by the patients.

TEAM-BY-TEAM ASSESSMENT

Team 1: RNA, RNP structure, fonction, maturation

Name of the supervisor: Bruno Charpentier (PR1 UL) & Iouri Motorine (PRCE1 UL)

THEMES OF THE TEAM

Team 1 has a long-standing expertise in the field of RNA biology, with a particular focus on non-coding RNAs (snoRNA, miRNA and lncRNA). Its thematics of research revolve around three main axes: the study of ribonucleoprotein complex assembly, the characterisation of RNA modifications and their impact on RNA metabolism, and the study of RNA/RNP functions in different contexts including pathologies (cancer, heart disease, arthritis…). The team has a strong know how in structural analyses and developed new methods to detect RNA modifications. It makes use of a valuable combination of genetic, proteomics and (epi) transcriptomics approaches.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has made a thorough response to the previous report recommendations and provides convincing evidence that these recommendations were taken into consideration, leading to effective improvements. Notably, several (9) publications have been co-published by different PI, suggesting tighter interactions between the team members and among the different axes of research. In addition, newly recruited team members have finalised their research programmes with publications as corresponding authors and participated in PhD supervision. Also, some efforts have been made to integrate cryo-EM in their structural studies, although the use of this technology still largely depends on external collaborations. While the team has attracted three foreign PhD thanks to a specific programme of the University, its appeal for international postdoc is still limited. Finally, in line with the recommendations, the team has considerably increased its participation in translational research project, organised a workshop on epitranscriptomics and reduced the duration of a PhD (from 4.5 years to 3.5).

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	3
Lecturer and associate lecturer	3
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)	7
Subtotal permanent personnel in active employment	**16**
Non-permanent teacher researchers, researchers and associates	1
Non-permanent research supporting personnel (PAR)	0
Post-docs	0
PhD Students	6
Subtotal non-permanent personnel	7
Total	**23**

EVALUATION

Overall assessment of the team

The team has an excellent level of production thanks to its high level of expertise as well as its important human and exceptional financial resources. It has established a very strong network of collaboration and could further extend its international standing. Altogether, the team is in an excellent position to pursue high levels fundamental scientific projects in the field of RNA biology and to increase its leadership. It is also well placed to consolidate its valorisation potential and could enhance its impact on health-related projects.

Strengths and possibilities linked to the context

Area 1: attractiveness
The international reputation of the team is excellent, notably thanks to its work on RNA modifications. The team is associated with the COST European network Epitran. It has developed fruitful collaborations with a very good European lab in Mainz (Germany) and another team in Leicester (UK) as well as with several reputable teams in France. Its international recognition is supported by invitations to write several reviews or methods book chapters, the participation to the organisation of six international conferences and the presence of two team members in the editorial board of good scientific journals.
At the national level, some team members are implicated in learned societies (SFBBM, sifARN) and/or evaluation board (CNU).
The team has attracted a very good number of PhD students (currently 4 PhD, 15 since 2016; for a supervision potential of eight HDR) and nine postdocs (including prolongation contracts for 2 former PhD). Three PhD students and one postdoc were foreigners.
The hosting policy of the team appears very supportive for the permanent staff members: researchers are encouraged to supervise PhD and as a consequence three obtained their HDR during the contract. In addition, two researchers/teacher researchers and two support staff were promoted.
The team has been extremely successful in obtaining financial support for its different lines of research. Overall, the budget of the team is very well balanced, with an excellent mix of resources, including a few international/European grants, five ANR (including 1 international and 1 as coordinator), two important grants from the Fonds Régional de Coopération pour la Recherche, and several grants from charities (including 6 from the Ligue régionale contre le cancer) or the University of Lorraine. Moreover, the team gained considerable financial resources thanks to its participation in clinical research projects, notably in the field of cardiovascular diseases (FEDER: Cohort Stanislas; RHU Fight Heart Failure; Institut de Cancérologie de Lorraine…). All the team members but one (C/EC) obtained some funding during this contract.

Area 2: production
The team production relies on very good standards and benefits from a wide range of state-of-the-art methodological skills (NMR and crystallography for structural studies, NGS-based techniques for RNA and chromatin studies, bioinformatics, RNAi and CRISPR/Cas9 for functional analyses…). Notably, the team has acquired some unique know-how and developed new NGS-based techniques to map RNA modification, expertise sought by diverse collaborators. The field of investigation is relatively wide but scientifically important and produced original results.
The team regularly published the results of its research in very reputed international scientific journals (68 original articles). In particular, team members were lead authors in 26 publications, including in Angew Chem, Mol Biol Evol, Nature Comm, Nucl Acids Res (5), as well as in more specialised but well-regarded journals (J Mol Biol, Human Mut, RNA, Structure…). In addition, they were associated with many high-profile publications (Angew Chem, Mol Cell, Nature, six Nat Comm, NCB, NAR, PNAS…) through collaborations, notably along the epitranscriptomic axis. They also contributed to seventeen review articles (including 1 Nat Rev Genetics), seventeen book chapters and ten clinical publications.

Area 3: society
The team has strongly increased its translational research activity, leading to the drafting of three inventions (one patent), one contract with a start-up company, and two projects in maturation/pre-maturation with the SATT. It is also associated with other IMoPA teams on two patents. Given the fundamental nature of the research lines developed in the team, this is a remarkable achievement and the interactions of the team with the socio-economic world are considered excellent.

Weaknesses and risks linked to the context

Area 1: attractiveness
Although the team has been particularly successful in obtaining grants, it might be difficult to maintain such a high level of budget on the longer term. Besides, its participation in European consortium could be increased.
Most of the postdoctoral fellows only spent around one year in the team, which was not sufficient to valorise their experience as most of them did not obtain a first author publication. Along the same line, some PhD students obtained their first author publication long after their PhD; although the quality of those publications was very good, such a delay might hamper their next career step.
Even though the clinician who joined the team in 2015 obtained some co-funding, co-supervised a PhD, and was promoted to PU/PH, he recently left the lab. This somehow questions the positioning of the clinical research projects in the team.
Although it might have been hampered by the COVID outbreak, participation in or invitations to leading international conferences in the field are not strong.

Area 2: production
Despite their strong financial resources, the clinical studies have not yet led to major discoveries and their articulation with the fundamental research projects of the team is not very strong. The departure of the PU/PH of the team could jeopardise some of the clinical projects.

Area 3: society
The team has limited outreach activities and does not sufficiently consider research dissemination as part of its activity profile (0%).

RECOMMENDATIONS TO THE TEAM

The team should maintain the high-quality production and level of funding of the team to gain further recognition and to increase leadership at the national and international levels.
The team could take further advantage of the team's expertise in epitranscriptomics and of the local platform to build an international network of excellence in this emerging field.
The team should pursue efforts to facilitate the access to and the use of cryo-EM.
The synergies between the different axes of the team could probably be further increased.
The team should consolidate its links with the socio-economic world and pursue its strategy of translational research. A more focused and impactful research plan in terms of clinically oriented projects should be envisioned as their current scope seems only remotely linked to the main interests of the team and do not fully beneficiate from its expertise.
The team should consider hiring/attracting (fewer) postdocs (but) on longer-term contracts (3 years and more) to maximise the benefits both for the postdoc and the team.
Given its scientific output, its expertise and its international standing, the team should try (1) to attract highly skilled international postdoctoral fellows susceptible of obtaining their own fellowships and (2) to participate more in EU-funded collaborative research programmes.
The outreach activities of the team should be developed.

Team 2:	Ingénierie Moléculaire, Cellulaire, Thérapeutique & Glycosyltransférases (MolCelTEG)
Name of the supervisor:	Sylvie Fournel-Gigleux (DR2 INSERM) & Mohamed Ouzzine (DR2 INSERM)

THEMES OF THE TEAM

The team has expertise in glycosciences, with a focus on glycosaminoglycans (GAGs) and their pathophysiological roles in interaction with collagen in the extracellular matrix and at the cell interface. Defect in the GAGs synthesis in rare genetic diseases that affect the connective tissue, osteoarthritis and breast cancer is investigated. The role of TMEM65 mutations in genetic diseases has been explored, more specifically its involvement in GAG chain polymerisation. Polymorphism of xylosyl transferase XylT-1 and syndecan 4 genes has been analysed in a Nancy CHU patient cohort in relation with the risk to develop osteoarthritis. Medicinal chemistry approaches have been pursued to find inhibitors of galactosyltransferase 7 for the treatment of mucopolysaccharidosis.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recruitment of one DR2 CNRS, one MCU UL and one technician UL has reinforced the team and shows clear institutional support. Two additional HDR should reinforce the supervision capacity of the team with defences scheduled in 2022. The collaboration with other teams in the unit has been improved and successful, resulting in several joined publications.
Investment in international conference presentations has been sustained. The team has organised an international meeting in Nancy. Three international networks have resulted in excellent publications with societal impact in the biomedical field. The newly appointed researcher is on international mobility and is already involved in international networks. The international mobility of early stage researchers remains low, with only two postdoc on international mobility including one arriving in 2021 with the new PI. There was no inclusion in European funded consortia during the period.
The methodology development of the Glyco-Fluo approach has been published, and acquisition of new equipment to support a platform development are anticipated within the new CPER contract. Specific recruitment to set up the platform has not yet been made.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	3
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)	3
Subtotal permanent personnel in active employment	**9**
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	3
Total	**12**

EVALUATION

Overall assessment of the team

The research of the Team is comprehensive and cohesive, tackling fundamental mechanisms, methodology development and medicinal chemistry. Unique models and expertise are available that also benefits to collaborations. At the national level, the team has a very good recognition for its contribution to the study of GAGs and glycosyltransférases related to their synthesis and contribute to strengthening this discipline. The team has proven its capacity for successful national and international collaborations with excellent teams. The specific contribution of the team to the study of the Ehlers-Danlos syndromes has led to very good communication to the public. The arrival of a new PI has the potential to increase the international standing of the team.

Strengths and possibilities linked to the context

The team has published eighteen original articles (with 3 from the PI joining in 2021) on the period, including seven as main co-author(s) (with 2 from the new PI) with five that can be considered major contributions to knowledge. These later publications corresponding to highlights of the team's research have been published in very good journals. Two of the co-authorship articles result from the successful collaborative ANR on TMEM65, with successive contract as partners (2015–2021 and 2021–2025) that show the interest of this project, given the competitive nature of the ANR calls. The team was a partner in a third ANR.
Team members have presented their research in eight international conferences and have contributed to the organisation of one international congress in Nancy on Glycans and proteoglycans, in direct connection to the team long-standing expertise. PIs of the team are collectively editorial board members in four good journals since 2019–2021. The international laboratory SFGEN with Dundee University, initiated during the previous contract, has been pursued and resulted in one key publication in a very good journal (oncogene) with interest extending to potential applications in human health. One PI of the team is an expert member on an international consortium on Ehlers-Danlos rare genetic syndromes, resulting in a review publication on classification recommendations (2017). An international collaboration with the Centre for Medical genetics of Ghent University, Belgium resulted in one publication as corresponding co-author of excellent quality and biomedical interest (Human Molecular Genetics).
As an example of the national stature of the team in the glycobiology field, the team has initiated a network of Glycobiology laboratories in the region Grand-Est that will increase the regional visibility of this research area.
Importantly, the team has successfully attracted a new PI, on an external CNRS DR2 position in international mobility. The newly appointed researchers have experience as group leader in a Max Planck Institute in Germany and joined the team in 2021. The new PI has already close links with the medical Faculty of Pueblo University in Mexico, through a LIA. In addition, institutional support to the team is strong, with the recruitment of a technician and a new MCU during the period.
Investment in PhD supervision by the two team leaders is excellent, with twelve theses overlapping the period and eight thesis defences. Three PhD students and two post-Doc were on international mobility.
Publications of the team are available in HAL repositories, contributing to the open science strategy. Very good efforts to communicate to the public on the biomedical aspect of the research project have been made, in the press and video interviews. Links to patient association and multiple financial supports by charities show the societal interest of the research. Very good valorisation efforts have allowed to attract a consequent financial support from the SATT Sayens and to publish one patent.

Weaknesses and risks linked to the context

Production remains modest, even for a small team, given that about half the articles are collaborative work and a majority is published in journals of specific readership. Ratio of PhD students versus publications is weak, with modest production for the PhD as first authors. Publication is strongly supported by the team PIs but remain more modest for some of its members if taking into account the authorship contribution.
The new PI already contributed to the publication production of the team by three articles, with two as principal investigator including one in the journal of general interest nature communication (last author 2021). However, given his late arrival in the contract, the published research concerns his work in the previous institute.
Funding of the team has been excellent, and the sources diverse, but remains limited if taking into account the high cost of recruitment of temporary researchers and engineers and the maintenance/renewal of the essential technologies. Arrival of a new PI is an excellent opportunity but it will remain to be demonstrated how the new

knowledge and expertise can be incorporated in the existing themes of the team. Only two international post-doctoral researchers joined the team, one with the arrival of the new PI in 2021.
Technological development within the team (Glyco-Fluo) is original. The method has been published and the needs (outside the Unit) for this approach will appear more clearly in the near future. The capacity to sustain a new platform remains uncertain based on the original glycol-technology, due to the size of the team and an unclear market for the approach at the (industrial and national) academic level.
Involvement of the team in European consortium of training and research has not succeeded despite some clear efforts.

RECOMMENDATIONS TO THE TEAM

Dissemination of the results from PhD students should be improved and accelerated to better support their career prospects because of the expected high standards. Continue the effort to increase the number of HDR holders within the team and to support the evolution to main authors of the junior team members in the publications.
There is a risk on the renewal of funding opportunities. Given the interest and quality of the team research, involvement as coordinators of national level grants need to be initiated. Effort to be included in European consortium needs to be pursued.
The balance between developing the team research projects and providing glyco-technological expertise to partner projects has to be carefully balanced because the publications related to the team's own research seems to be of higher quality than some of the collaborative work. The weight for the team to develop a bona fide platform versus the collaborative work that still could be pursued needs to be carefully weighed. That point could be solved by externalising the technological aspects to a platform, with dedicated personnel, that would benefit from the team original technological expertise.
As demonstrated during the period, the international collaborations resulted in excellent scientific production and their reinforcement should be privileged. The dissemination of the work at the international level needs to be sustained to facilitate this process.

Team 3: Enzymologie Moléculaire & Structurale (EMS)

Name of the supervisor: Kira Weissman (PR1 UL) & Sandrine Boschi-Muller (PR1 UL)

THEMES OF THE TEAM

Team 3 is composed of the PKS and Redox groups which are two independent groups since 2019.
Therefore, the review of Team 3 will be divided in two parts.
The PKS group focuses on the structure-function relationships of polyketide synthases enzymes with the help of a large panel of complementary approaches (such as enzymology and structural biology – X-ray crystallography, NMR and Electron microscopy). The knowledge that is built can be applied to the production of molecules of pharmacological interest.
The Redox group is studying the molecular and cellular mechanisms associated with different pathophysiological processes involving enzymes that depend on the chemistry of sulphur.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Despite the recommendations of the previous report concerning the need for, 'direct collaboration between the axis of team 3', both groups stayed independent and answered separately to the recommendations.
The PKS team arguments were very convincing and without any doubt they successfully answered all the points raised of the previous comity. They made substantial effort towards their first cryo-EM structures of PKS through collaborations. They made an excellent increase (as coordinator or co-head) in the integration to national (3 ANR including one with a company) and international networks (2 international ANR – Germany and Switzerland – and the IRAADD network; 36 research teams from 14 countries). This is also valid for translational research with the co-direction of the Biomolecules IMPACT project (17 academic laboratories and as many industry members). Finally, they increased their overall visibility by co-organising several international conferences or through excellent publications (3 publications and two reviews in high impact journals).
The Redox team answered the concerns of the previous report in most cases. They established complementary techniques (*cellulo* scale) by recruiting a new specialist and initiated with him a move towards a subject more relevant to human health. The team increased its network of collaborators in France with substantial financial public supports (several local grants, two ANR) and six SATT funding. On the other hand, the team only slightly increased its international network. Finally, they increased their overall visibility through original publications (4 publications with high visibility).

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	2
Lecturer and associate lecturer	6
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)	3
Subtotal permanent personnel in active employment	**12**
Non-permanent teacher researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	0
Post-docs	1
PhD Students	6
Subtotal non-permanent personnel	7
Total	**19**

EVALUATION

Overall assessment of the team

The PKS group has an excellent level of scientific production. Its original expertise attracted world class international collaborators in the field of PKS and the potential of its research attracted excellent funding for projects and students. On top of this academic excellence, the team is very active towards the potential biotechnological applications of its research through partnerships with non-academic actors.
The Redox group has a very good level of scientific production. It has attracted a new teacher researcher that will boost its in cellulo expertise. The team has succeeded in obtaining large funding for both research projects and PhD students, in particular through its outstanding success in getting SATT funding.

Strengths and possibilities linked to the context

PKS
The team is composed of five permanent staff members and holds an excellent publication record with co-authorship in two large reviews and three articles as last author in valued journals (Two *Nature Communication and one* JACS).
The team has an excellent national and international visibility notably with the coordination of five ANR (including two international ANR with world-class scientists) and its participation to the JPI-AMR translational network IRAADD (36 research teams from 14 European and non-European countries). Altogether, this represents an enormous improvement in the visibility of the team compared to the previous period. The team was also very well represented at international meetings as a speaker or as an organiser (more than 15 invited seminars and participation to the organisation of five international conferences).
The team has been able to recently recruit, by local mobility, a new MCU and during the period one of the MCU published his HDR. This increases the supervision capacity of the team that currently already attracted a very good number of PhDs and postdocs (7 PhD and 5 postdocs including 2 international and 2 former PhD). All PhD students published an article in first position, showing the commitment of the team towards quality of training and supervision of their students.
The team has boosted its translational research activity with its integration to large networks. The PI is for example the co-director (since 2015) of the Biomolecules of the LUE where she is co-heading one of the projects work packages on polyketides. The team has also initiated collaborations that are now secured in the long term with two small French companies (Plant Advanced Technologies and Abolis Biotechnologies). Altogether, the team was successful in obtaining large financial support for its research in the last period (for a total of> 1.3 million euros) and in securing close collaboration with two companies. With three recent ANR (ANTHRALAB, PKSOx, NRPSBacAza), the team can enter the next contract with assurance. The lab produced excellent research and maintained their high level of fundamental interdisciplinary research. They are ready to move towards the electron-microscopy bright future of their research topics.

Redox
The team is composed of seven permanent staff and holds a very good publication record with sixteen publications in peer-reviewed journals including four articles as first and/or corresponding author in high visibility journals (one *Nat. Chem. Biol*. and three ACS catalysis).
The team has an excellent local and national visibility notably with the coordination of two ANR and a large network of local and national collaborators that gave rise to several co-publications through the involvement of the group in the B2S platform of the UMS. These collaborations allowed access to complementary approaches such as mass spectrometry or atomic force microscopy. The team was also well represented at national meetings as speakers (11 presentations). On the human resource aspect, the team had a very good performance with the promotion of the only full-time researcher as a CNRS research director and the recruitment of a new teacher researcher. The incoming teacher researcher brings an *in cellulo* know-how (yeast and human cell) that complement very well the *in vitro* enzymology expertise of the team. This new MCU is allowing reshaping part of the team projects towards redox regulation in humans (one project around Alzheimer's disease and one around the inactivation of Norovirus, with international collaborators). Altogether this represents a real improvement in the national visibility of the team compared to the previous period. The team was also represented at international meetings as speakers (7 seminars).
Two MCU should finish their HDR to increase the supervision capacity of the team who attracted a very good number of PhDs and postdocs (6 PhDs and 5 postdocs including 3 internationals). All PhD students published an article in first position, once again showing the commitment of the team towards proper training and supervision of their students.
The team has made an impressive boost in its translational research during the period. First by its integration and active work in networks such as IMPACT 'Biomolecules'. They are there either work package leaders or partner

in a network with thirteen other regional laboratories. Second by its outstanding success in getting six SATT funding to develop their innovative ideas.
Altogether, the team was successful in obtaining large financial support for its research in the last period (for a total of> 1.1 million euros).

Weaknesses and risks linked to the context

PKS
The team is composed of five (soon six) permanent staff, the smallest group of ImoPa. It comprises only one IE and no full-time researcher. Even if it has one of the best publication ratios of ImoPA, it might be difficult to keep this level of publications in the long run without the recruitment of a full-time researcher.
The majority of the team production (publication, grant coordination, participation in networks and international recognition of the team) comes from the team leader only. This creates an imbalance between her and the rest of the team. Indeed, even if they are sometimes co-corresponding, few teacher researchers signed a publication as last author.
Despite its implication in several networks and its effort in writing grants, the team has not managed to integrate a European consortium of research or training (MSCA DN).

REDOX
Almost all the contracts of the team (local, ANR, SATT…) will be finished before the end of 2022 and there is no significant funding mentioned in the report to sustain a similar level of research in the future.
The team still lacks proper international recognition (few invited seminars at international conferences and few international collaborations).

RECOMMENDATIONS TO THE TEAM

PKS
The team should try to improve or at least keep the very good momentum of the last period by continuing its excellent research in Nancy and its fruitful collaborations with its national and international partners. It should persist in its attempt to recruit permanent researchers and should keep its participation in writing European project and training grant applications. They should consider that the various collaborations with companies could be a lever to apply and enter with them one 'SME driven' European call.
The team leader should increase support for teacher researchers to develop their own research projects so that they become more independent and enter new networks or get their own research funding for the team.
Finally, the team should keep its spirit of publishing a rather high-quality, high-impact publication versus increasing the quantity of its publications.

REDOX
The team should continue its excellent research in Nancy. The team must extend its national collaborations to the international level and try to participate to European project and training grant applications.
The team should improve its international networking and intensify its efforts to secure the funding of the coming years.
Finally, the team should try to publish a rather higher-quality, high-visibility publication versus increasing the quantity of its publications. This might mean to decrease or rationalise its implication in the B2S platform of the UMS and use this time on the most promising project of the team.

Team 4:	Inflammation, Dérégulation Phénotypique & Remodelage Articulaire Pathologique (IDePRAP)
Name of the supervisor:	Jean-Yves Jouzeau (PU-PH1 UL) & Pascal Reboul (PR2 UL)

THEMES OF THE TEAM

The research field of Team 4 is centred on the pathophysiological mechanisms of osteoarthritis and related chronic inflammation. Additionally, a molecular link was identified between joint and bowel inflammation, by showing notably the role of PPARγ in these processes. Finally, The WNT pathway was studied in the context of osteoarthritis, and peptides altering WNT signalling were characterised as pharmacological tools for therapeutic interventions.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team should focus on specific projects in which the team can be of world class. The team should try to improve scientific output, number and impact factor of articles in international peer-reviewed journals.
This recommendation is achieved.

The team should expand its international network to become involved in grants at the European level. Improving the funding of the team should be of the highest priority. Team members should also try to attract more postdocs, at least one per axe, who stay longer than a year.
The team obtained a high number of international and national grants. However, international visibility is still moderate. Several postdocs were hired.

More effort should be put into the relationship with (big) pharma. The development of an attractive website will improve the communication with the general public.
Both recommendations were achieved.

The expert committee recommends trying to decrease the burden on management and teaching and reallocate this time to research; improve the interaction between the different axes since combined efforts can result in larger quantity and better quality of scientific output.
At UL, discharge of teaching duties is only possible in the first year of recruitment. Coordination and exchanges between axes were not strengthened, however scientific output is excellent for the three axes (see below).

Put effort in attracting more PhD students.
The lack of PhD students is even worse (only one ongoing PhD student in December 2021).

The team should focus on the scientific niches in which they can be leaders. This could be achieved by acting on the crossroads of the different research axes. Since some of the PIs have good connections with the hospital and biobank, the expert committee recommends increasing efforts in translational research and the studies on patients. Securing funding should be a top priority. The number of projects should not be too diverse, and the team should combine strength by collaboration between axes.
Translational research has been developed, and the team capacity to obtain funding is excellent.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	4
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	4
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	3
Subtotal permanent personnel in active employment	**12**
Non-permanent teacher researchers, researchers and associates	1
Non-permanent research supporting personnel (PAR)	1
Post-docs	1
PhD Students	1
Subtotal non-permanent personnel	4
Total	**16**

EVALUATION

Overall assessment of the team

The research studies performed are of high scientific interest, with important potential medical benefits. The Team is in a very good dynamic since last evaluation, both for the scientific production and for their success in the valorisation. The team produced cutting-edge data, published in very good to excellent journals and characterised pharmacologic tools that generated industrial interests. Altogether, it is a very good team, with only two weaknesses; national and international visibility is not at the level of its scientific production, except for one member and the number of PhD students is too low, with poor supervision capacities.

Strengths and possibilities linked to the context

The three main research projects of the team are scientifically connected to each other, and all three are highly productive in terms of scientific and medical advances, publication and valorisation. The biological mechanisms in OA are well explored and the researchers developed original concepts, with a good connection to the clinic and to valorisation partners.
The team staff is well equilibrated with four full-time researchers, one professor, one associate professor, three medical professors and three engineer/technicians. Six postdocs were hired during the last six years, which is good for a team of this size.
Most original articles are published in middle to high range journals (39 out of 51). The publication level per PI is high (5.7 original publications per PI). In addition, the team published nineteen reviews and 27 clinical articles that are valuable contributions to their respective scientific and medical domains. Altogether, the publication level is remarkable.
The valorisation is also very active, with four patents filed and three industrial maturation projects with SATT SAYENS.
Members of the team were also involved in three clinical trials, which shows their commitment into the clinics.
One PI was invited in multiple international and national meetings.
The team supervised eight PhD students who defended their thesis since 2012. The average publication level is two per student, one as first author on average, which is low. However, articles were generally published in

middle-high range journals. Two students were also co-authors of filed patents, and four were co-authors of reviews. All but one post-docs (only 2 months stay) hosted by the team published at least one article during or within the next year of their stay. Those hosted for more than 22 months (2 post-Doc) published at least one original article as first author in international peer-reviewed journals.

Members of the team participate to editorial boards of scientific journals and/or are part of the scientific board of four French scientific societies, which are good signs of recognition and of inclusion into networks.
The team has a very high capacity to obtain grants from various sources and to support its fundamental and translational projects. Altogether the team was funded by an international and three European grants (for a total of 422.5 K€), by 1 ANR (74 K€), five PIA (416 K€), by seven subsidies from regional collectivities (706 K€), four from associations/foundations (132 K€), six from Lorraine University or CNRS (115 K€), five from the CHRU (421 K€), five from SATT maturation projects (837 K€) and three industrial contracts (154 K€) during the 2016–2021 period.

Weaknesses and risks linked to the context

The team only formed a low number of PhD students during the last period, and there was only one PhD student in December 2021. This is a weak part of the team. Among the 8 PhDs defended, two students published a review and not an original article as first author (but one is co-author of a patent that may be followed by a publication).
There are only four HDRs among the nine PIs, and one for an engineer.

RECOMMENDATIONS TO THE TEAM

The major recommendation is to keep and even increase the level of production in the future contract to reach top range journals.
PIs should participate more frequently to meetings, as a way to increase their visibility and to initiate collaborations.
The number of PhD students is far too low for a team that includes nine PIs. More HDR could be obtained, especially by full-time researchers. This could potentially lead to more PhD students, who constitute vital forces in research. Increasing the number of PIs with HDR would raise the possibility to present candidates at the 'Ecole Doctorale'. Additional sources of financing students should be explored.
A possible risk of excessive diversification between the three-research axes may occur and should be considered.
As pointed by self-evaluation, the frequency of lab/team meetings is too low. They are mandatory to increase the scientific knowledge of the team members, to allow information transfer between members of different axes and to increment the presentation capacities of the students.

Team 5:	Bioingénierie, Médecine Régénérative & Caractérisation Tissulaire (BioReMaTCh) »
Name of the supervisor:	Astrid Pinzano (DR2 CNRS) & Patrick Menu (PRCE2 UL, emeritus since 2020)

THEMES OF THE TEAM

The research field of Team 5 is highly interdisciplinary, based on the complementary skills of researchers, teacher researchers and clinicians from various backgrounds. The themes of research are organized in two main work packages: regenerative medicine (WP1) and characterisation tools (WP2). The team studies are focused on osteoarticular pathologies and cartilage regeneration/reconstruction but also include vascular engineering and the use of specific sources of stem cells (from synovial fluid, dental pulp or umbilical tissues) for tissue engineering and regenerative medicine. The characterisation of in vitro reconstructed tissues as well as normal and pathological in-situ tissues offers many assessment tools for the repair of degraded tissues before and after treatments.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

R1#: The team might want to explore the possibility to limit its thematic diversification to focus its manpower on the most innovative topics and view as a challenge to publish in the highest-ranking journals.
This recommendation has been partially achieved. The Team still has research topics both in soft and hard tissues creating different types of problem-solving approaches when it comes to tissue engineering. The level of publication is excellent.

R2#: Team 5 should view as a challenge to obtain funding of large-scale projects at the European level.
Funding of large-scale European projects remains an issue, no strategic plan related to European funding seems to have emerged. The team relies more on an opportunistic strategy in this matter. If efforts have been made to apply to these types of projects, no positive outcomes have been seen so far.

R3# Strengthen its communication with the general public will help team 5 to further disseminate its knowledge to the laymen. A further increase of collaborations with private companies may provide additional resources.
The involvement of the team in communication towards the general public is higher than average but strong collaborations with private companies are still lacking.

R4# On the whole, an appropriate balance between administrative tasks and research projects should be reached.
This recommendation has been taken into account but the time invested in funding applications and instruments overseeing still seems significant.

R5# The team has an excellent expertise and record of training students through research. The team should view it as a feasible challenge for the next five years to transfer its expertise at the European level.
This recommendation has been partially achieved. The participation to the Procope PHC programmes is a good omen for future projects.

R6# The team might want to strengthen its strategic plan by selecting their most innovative topics to bring them to a level of international excellence.
This recommendation has been partially met. The publication level, although already excellent could be further improved by strengthening international collaborations and participation to international networks.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	4
Lecturer and associate lecturer	4
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)	5
Subtotal permanent personnel in active employment	**15**
Non-permanent teacher researchers, researchers and associates	2
Non-permanent research supporting personnel (PAR)	0
Post-docs	2
PhD Students	5
Subtotal non-permanent personnel	9
Total	**24**

EVALUATION

Overall assessment of the team

The research studies performed in Team 5 are excellent, with an ideal setting for the rapid translation from bench to bedside. The scientific production of the Team is excellent, and all members contribute to the publication effort to demonstrate a great dynamism regarding the communication of scientific results.
The local and national collaborative network of the Team is impressive. The links with several other laboratories from the Université de Lorraine is a strength but it also points at a major weakness, the lack of presence in international projects and calls. An effort has been done to apply to more international programmes, so far without positive returns, the team should pursue its efforts to be inserted in or lead international programmes.

Strengths and possibilities linked to the context

The structuration of the Team in two work packages (WP1: 'Regenerative medicine' and WP2: 'Characterisation tools') defines well the research specificities of the Team with strong possible interconnections.
Strong links with the CHRU of Nancy supports the development of translational research in both WPs of the Team.
The team composition is well balanced with two full-time CNRS researchers (DR2 and CRCN), three full-time medical professors (+ one at 50 percent and one associated with the team), one associate professor, three medical associate professors. The number of scientific supporting staff is unusually high with five engineers/technicians. The team also seems to be attractive for students (15 PhD students over the period even if two medical students dropped out).
The scientific production is of excellent quality in terms of number of publications (56 scientific publications, 14 reviews, and 93 clinical articles), as well as in terms of quality (17 publications with impact factor ≥5 and 4 ≥10, including one with an impact factor of 16,971). Notably, a large part of the scientific articles (33) involves other IMoPA teams. This point added to a very large collaborative network within UL highlights the extremely good integration of the team in its local environment.
The production of the young scientists (PhD and postdoc) is also important (3.4 publications per PhD student).

The Team has a balanced activity in most of the categories of the activity profile. The contribution to innovative teaching could have been highlighted more since the team reports the production of podcasts and videos to teach pharmacology to medical students.

Weaknesses and risks linked to the context

The field of tissue engineering and regenerative medicine is highly competitive.
The team is under average in the unit activity profile in the valorisation, transfer and innovation category. Despite some very innovative aspects of their research, it is not clear if team members really have an active policy to protect potential inventions and bring them to the clinical applications. A patent could not be filed because of previous disclosure. No strong collaborative work has been performed with industrial partners. The research project funded is always in low TRLs (POC towards TRL2-3).
The level of funding of the team is relatively low considering the number of permanent positions with a predominance of contracts <50 K€.
There is a large discrepancy between the recognition of the Team on a local and national levels and the international level.

RECOMMENDATIONS TO THE TEAM

Define a specific strategic plan for applications to international calls. PHCs, Erasmus plus are projects that help create a network of collaborators. Interreg projects and bilateral ANR projects (PRCI) can also be a good start for European funding, especially considering that team 5 has a strong local presence and an ongoing collaboration with Germany. Once this level is achieved larger projects can be submitted. The opportunistic approach has its limits and does not allow a more strategic and constructed development.
The researchers of the Team should be more present in international (European) scientific societies (ESB, ETRS…) both participating and being members on boards or organisation committees to increase the Team's international visibility.
The effort to focus on a more limited number of scientific themes should not loosen. The research in two WPs as proposed is indeed the ideal structure as long as the two WPs are interconnected and feed each other.
Non-academic collaborations (and more specifically with companies) should be developed much further. Specific targeted goals such as a CIFRE PhD, BPI-funded projects, ANR PRCE with a company should be defined for the next evaluation.
The contact with the SATT should help define the most translational projects, patentable research products and partnership with local or national companies.
The team should already prepare for the renewal of its senior researcher by attracting young PIs as well as full-time scientists.
As the team develop a true regenerative medicine scope with a large spectrum of approaches, from the characterisation of the pathologies to their treatment with stem-cell based tissue engineering, they should build more on this strength to increase its socio-economic impact.

Team 6:	Ingénierie Cellulaire, Immunothérapie Cellulaire et Approches Translationelles (CECITA)
Name of the supervisor:	Danièle Bensoussan (PU-PH1 UL) & Marie-Thérèse Rubio (PU-PH2 UL)

THEMES OF THE TEAM

The team's main objective is to develop new cell therapies for the treatment of diseases such as infections (septic shock, COVID-19, viral infections after haematopoietic stem cell transplantation HSCT), graft-versus-host-disease (a complication of HSCT) and leukaemia. Its work extends from the identification of appropriate cell types and their thorough characterisation to the development of new clinical-grade production protocols and the validation of their therapeutic applications in various preclinical models and in clinical trials. In this context, the potential of several cell types has been explored: Wharton's jelly MSCs, iNKT and CAR-iNKT cells, myeloid-derived suppressor cells (MDSCs), CAR T-cells and NK cells.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The main recommendations of the previous report were linked to the feasibility of the project in view of technical considerations (clinical grade expansion of iNKT cells, biomechanical studies), of the high number of cell types and pathologies under consideration, of the size of the team and its high teaching or clinical load.
The recommendations were achieved for the largest part:

- A new method to expand iNKT cells has been developed and patented; new developments involving iNKT cells are under consideration such as the genetic introduction of a chimeric antigen receptor (CAR-iNKT) to treat acute myeloid leukaemia.
- The number of cells/pathologies remains high and this probably limits thorough mechanistic studies but the team has shown its capacity to develop interesting applications in the various selected fields.
- The team size has been increased, especially with the recruitment of five MCU-PH. Team 6 is thus presently composed of four PU-PH, five MCU-PH, one PR, one MCU, one emeritus DR CNRS and one scientific supporting staff.

The biomechanical studies have not been pursued. The main recommendation which has not been possible to follow is the recruitment of a full-time scientist and this recommendation will be renewed for the next contract.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	5
Lecturer and associate lecturer	6
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	0
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	**12**
Non-permanent teacher researchers, researchers and associates	1
Non-permanent research supporting personnel (PAR)	2
Post-docs	0
PhD Students	8
Subtotal non-permanent personnel	11
Total	**23**

EVALUATION

Overall assessment of the team

The team has shown its capacity to handle a relatively high number of pathological conditions (septic shock, allogeneic haematopoietic stem cell transplantation, COVID-19, cancer) and cell types (MSCs, iNKT, MDSCs, VSTs, CAR-T, NK cells) and has achieved very significant developments in all areas with several validated clinical applications and industrial developments. The productivity of the team related to this work is very high in terms of number of publications with high therapeutic potential. The publication level could, however, be increased and have a stronger mechanistic focus to better fit the academic standards of CNRS-University-supported teams.
The collaborative activity of Team 6 is very high, especially at the national level and through a very productive partnership with Chinese labs. Additional international collaborations (outside China) could help to mitigate the present limitations due to the unstable COVID situation in China, increase the publication level and find additional funding sources.
The team possesses various types of skills, but they are mainly in the medical field and they could be better balanced by more basic science expertise in immunology and bioinformatics.

Strengths and possibilities linked to the context

The translational activity of Team 6 is excellent with six ongoing clinical trials, three filed patents and the creation in 2019 of the StemInov start-up based on one of these patents (3 employees). It benefits from the close links with the cell therapy unit of Nancy CHRU (to which several team members are connected for their clinical activity) and from the industrial integrator MTInov.
The scientific production of the team is very high (84 scientific articles, 73 clinical articles, ten reviews and fourteen book chapters) and reflects the involvement of team members in both scientific and clinical activities. All researchers/teacher researchers were authors of several publications during the evaluation period despite the fact that they all have heavy clinical or teaching duties.
The training activity of Team 6 is quite significant with ten PhDs who defended their thesis in the 2016–2021 period, and eight ongoing PhD students. Eight PIs have an HDR, and five of those PIs supervised PhD students during the 2016–2021 period.
In general, Team 6 is involved in several collaborative studies both at the national and international levels. A long-lasting partnership with China has been further reinforced in the past years through the involvement of new teams (7 from France and 7 from China) and the establishment of an International Research Network coordinated by a Team 6 member. This provides interesting opportunities for international exchanges and funding.
The team also collaborates on a regular basis with Team 5 inside IMoPA (more than 10 common publications). Interactions with other teams seem to be more limited.
The team seems to have a very solid reputation in terms of immunomonitoring as illustrated by its involvement in several translational industrial and academic collaborations in the field of allogeneic haematopoietic stem cell transplantation (one of its core topics) but also in cancer or severe COVID-19 infection.
Team 6 is well funded. It has been especially successful for getting money through charities and also from ANR and INCA. Notably, the strong partnership with China also gives very valuable funding opportunities for the team. The team also recently obtained new resources through a maturation project from the SATT SAYENS.

Weaknesses and risks linked to the context

The level of published scientific articles is not as high as it could be in the field of immunology with a few exceptions (Leukaemia 2017, J. Hematol. Oncol. 2017, Oncoimmunol. 2018). Most articles are in collaboration, and only a small proportion of the publications are signed by a Team 6 member as last author.
The clinical studies seem to outweigh research on biological mechanisms, while it would be expected for an academic lab supported by a University and CNRS to produce more basic science.
All team members have high loads of teaching or clinical activity which certainly impair their commitment to research.
Only a few publications simultaneously involve the two main PIs of the Team, suggesting that synergy inside the team may not be optimal.
The average number of original publications per PhD student who defended their thesis is 2.6, which is correct, among which 1.3 were signed as the first author. However, this number is highly variable between students, with three students having no first-author original publication. Nine out of ten PhD students did not pursue in science, which indicates that the training did not lead to a scientific career.

The two hired postdocs did not bring much scientific input when looking at their publication level.
Collaborations within CESMER IRN are impacted by the COVID situation in China and might be less productive in the future.

RECOMMENDATIONS TO THE TEAM

The team should aim at increasing its publication standards and the number of publications with leader positions. As suggested in the self-evaluation, this could be achieved through more mechanistic studies and the recruitment of at least one full-time scientist who would have more time dedicated to research. Another approach could be to refocus the team's projects on a smaller number of applications and to allocate more human resources to these projects. The PhD students could be better valorised to produce more scientific data. A selection of high-potential PhD students/postdocs will thus be a critical point in the future.
Another valuable input, given the type of research performed by Team 6, would be to recruit an engineer or a researcher trained to run bioinformatic analyses of single-cell/multiparametric omics data.
International visibility could be further extended by the broader participation of team members to international and less specialised meetings and learned societies.

CONDUCT OF THE INTERVIEWS

Date(s)

Start: 21 septembre 2022 à 8 h

End: 21 septembre 2022 à 18 h

Interview conducted: on-site or online

INTERVIEW SCHEDULE

Ingéniérie Moléculaire et Physiopathologie Articulaire (IMoPA)

Director: Jean-Yves Jouzeau
Deputy-Director: Bruno Charpentier

Program of the HCERES Interview

September 21, 2022
Nancy

HCERES Scientific Officer
Marie José Stasia marie-jose.stasia@hceres.fr Tel : 33 (0)6 80 51 89 32

8:00–8:15 Testing Zoom connections

8:15–8:30 Closed session Expert Committee (EC)–Scientific Officer (SO)

Assessment of the Unit, Scientific Plenary session

8:30–8:45 Presentation of the EC to the staff members by SO

8:45–9:30 Presentation of the unit by Jean-Yves Jouzeau (30 + 15 min discussions with the committee)
Attending: EC, SO, all the unit members

Presentation of the teams

9:30–9:50 Team 1: RNA-RNP Structure Fonction Maturation (Bruno Charpentier, Iouri Motorine)
(15 min presentation +5 min questions)
Attending: Team members, EC, SO, director of Unit

9:50-10:10 Team 2: Molecular, Cellular, Therapeutic Engineering and GlycosylTransferases (Sylvie Fournel-Gigleux, Mohamed Ouzzine and Guillermo Barreto)
(15 min presentation +5 min questions)
Attending: Team members, EC, SO, director of Unit

10:10-10:30 Team 3: Structural and Molecular Enzymology (Sandrine Boschi-Muller, Kira Weissman)
(15 min presentation +5 min questions)
Attending: Team members, EC, SO, director of Unit

Break 15 min
Closed session Expert Committee (EC)–Scientific Officer (SO)

10:45-11:05 Team 4: Inflammation, Phenotypic dysregulation and Pathological Joint Remodelling (Jean-Yves Jouzeau, Pascal Reboul)
(15 min presentation +5 min questions)
Attending: Team members, EC, SO, director of Unit

11:05–11:25 Team 5: Bioengineering, Regenerative Medicine & Tissue Characterisation (Reine El Omar, Astrid Pinzano)
(15 min presentation +5 min questions)
Attending: Team members, EC, SO, director of Unit

11:25–11 h 45 Team 6: Cellular Engineering, Cellular Immunotherapy and Translational Approaches (Danièle Bensoussan, Marie-Thérèse Rubio)
(15 min presentation +5 min questions)
Attending: Team members, EC, SO, director of Unit

11:45–13:30 Lunch Break

1:30 p.m.–14:00 Meeting of the Committee (closed hearing)

2 p.m.–2:30 p.m. Technical and administrative personnel
Attending: Technicians, Engineers, Administrative staff, EC

2:30 p.m.–15:00 Thesis students and postdocs
Attending: PhD students and postdocs, EC

3 p.m.–3:30 p.m. Researchers and teacher researchers
Attending: Researchers and teacher researchers except group leaders, EC

3:30 p.m.–16:00 Meeting of the Committee (closed hearing)

4 p.m.–4:30 p.m. Meeting with the representatives of CNRS and University
Attending: expert committee, representatives of Institutions, SO

4:30 p.m.–17:00 Meeting of the Committee with the head of the unit
Attending: Unit Direction, expert committee, SO

5 p.m.–6 p.m. Meeting of the Committee (closed hearing)

GENERAL OBSERVATIONS OF THE SUPERVISORS

UNIVERSITÉ DE LORRAINE

Nancy, March 17, 2023

Direction de la Recherche et de la Valorisation

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Objet : General comments on the evaluation report - DER-PUR230023164 – IMoPA (Ingénierie Moléculaire et Physiopathologie Articulaire).

Dear Sir or Madam,

Thank you for the evaluation report made for the research unit IMoPA (Ingénierie Moléculaire et Physiopathologie Articulaire), that you sent us on February 20, 2023. I would also like to sincerely thank the evaluators for the quality of the exchanges and for the analysis of this research unit.

Please find attached the general observations made by the unit on the evaluation report submitted.

Thanking you again for this evaluation which will allow the joint research unit IMoPA to continue its reflection on the basis of the recommendations made, please accept, Madam, Sir, the expression of my respectful greetings.

The Vice President of the Scientific Council,

Alain HEHN

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General comment for team 2

P10

Strengths-last lines

IMoPA contributes to the steering of the supervising bodies by participated as invited member to CNRS committee **section 20** (sfg)

Weaknesses

An updated English version of the website is ongoing.
Internal seminars have been scheduled for 2023 and take place in a larger auditorium located on the campus.

P12

Scientific advances have been made by Team 2:

Team 2 identified the Mn2+ transporter TMEM165 a new player in proteoglycan synthesis (**Cell Death and Disease 2021**), demonstrated that chromatin opening during transcriptional initiation involves DNA break intermediates followed by DNA repair ensuring genome integrity (**Nat Comm 2021**), provided interesting results on the non-canonical Wnt signaling in OA (**Cell Death and Diff 2018**) and identified the heparan-sulfate sulfotransferase 3-OST3A as a marker of HER2+ breast cancer aggressiveness (**Oncogene 2016**).

3) One PhD student (R. Diana) participated to the regional competition "my thesis in 180 seconds" for popularization of science.

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- Concerning post-docs contribution to the team: although not yet recruited, funding for a post-doc on ANR (ENIGMnca) has been obtained, the candidate should soon join the team.

- A larger sharing of the supervision duty within the team might facilitate the process is recommended.

It has to be mentioned that several PhD theses have been and are co-supervised.
PANG X 2016: sfg/Gulberti S, GAUCHE C: 2016 sfg/Gulberti S, KHAN S 2020: MO/Barré L, DIANA R ongoing: sfg/Bui C, SWAMINATHAN G (ongoing): Barreto G/Gulberti S, ROGEL AYALA D (ongoing): Barreto G/Braun T

General comment for team 3 PKS group

We thank the expert committee for their encouraging evaluation of the group. Nonetheless, we would like to take the opportunity to address several points, as follows.

1. Comment: 'Indeed, even if they are sometimes co-corresponding, none of the MCF signed a publication as last author'.

Response: Christophe JACOB MCF was last corresponding author on a paper published in *Chem. Commun.* in 2020 (doi.org/10.1039/D0CC05068G), which was duly cited in Annex 1. He will also be the last corresponding author on an article based on the work of the PhD student Li SU, whom he co-supervised. It is also worth noting that Arnaud GRUEZ MCF is last corresponding author on a paper currently in press with *Nat. Commun.* (see https://www.researchsquare.com/article/rs-2103032/v1 for the open access preprint; doi: 10.1038/s41467-023-36974-3 for the final version), and Benjamin CHAGOT MCF will be last corresponding author on an article in preparation. Thus, this issue is being addressed progressively.

2. Comment: 'The vast majority of the team production (publication, grant coordination, participation in networks and international recognition of the team) comes from the team leader only'.

Response: We would like to reiterate that A GRUEZ was the named partner on the ANR SMALA (ANR-21-CE07-0061-02, €182 k), and has coordinated all interactions with the grant PI, Anne ZAPARUCHA, managed the budget, etc. In addition, every primary publication from the group included at least one MCF if not two, as co-corresponding author.

3. Comment: 'Despite its implication in several networks and its effort in writing grants, the team has not managed to integrate a European consortium of research or training (MSCA DN)'.

Response: We would note that team head Kira WEISSMAN is since 2022 co-coordinator with Stephane DESOBRY of a new Erasmus program to be launched in 2024, called Biomolecules and the Bioeconomy (BioMolEc). The Erasmus includes 5 international partners (University of Copenhagen, DK; Universidad Politecnica de Valencia, ES; University College Dublin, IR; Leibniz University Hannover, DE, and University of Athens, GR).

4. Comment: 'The team leader should help its MCF to develop their own research projects so that they become more independent and enter new networks or get their own research funding for the team.'

Response: This comment is understandable in view of the fact that we did not directly address the MCF's research projects in the dossier. However, all of the MCFs started to develop independent projects during the evaluation period, and obtained associated funding. Specifically, as duly noted in Annex 1, in addition to the ANR SMALA cited above, B CHAGOT and C JACOB were awarded grants for 'Projets incitatifs' by respectively the Pole BMS and AAP-LABEX Arbre (€15 k and €4.5 k). C JACOB's project notably includes academic collaborators based in Italy and Germany. Lynn PAURON who joined the group in January 2022 is also establishing an independent line of research anchored in molecular dynamics. These projects will be pursued with the assistance of KJ WEISSMAN, with the objective of obtaining sufficient preliminary data to allow for further larger-scale funding applications (e.g. to the ANR).

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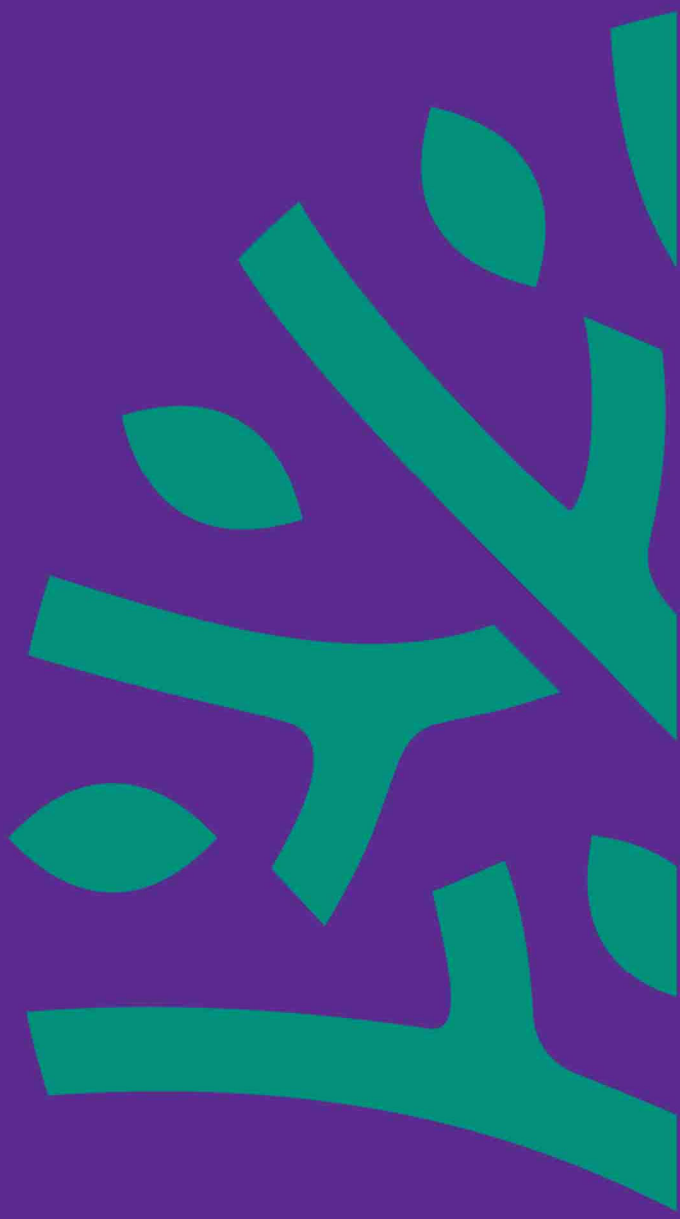

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