

EVALUATION REPORT OF THE UNIT  
NanoRegMed – Nanomédecine régénérative

UNDER THE SUPERVISION OF THE  
FOLLOWING ESTABLISHMENTS AND  
ORGANISMS:

Université de Strasbourg  
INSERM

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**EVALUATION CAMPAIGN 2022–2023**  
GROUP C

Rapport publié le 12/06/2023



In the name of the expert committee<sup>1</sup>:

Frédéric Mallein-Gerin, Chairman of the committee

For the Hcéres<sup>2</sup>:

Thierry Coulhon, President

Under the decree n° 2021-1536 of 29<sup>th</sup> November 2021:

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

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

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

## MEMBERS OF THE EXPERT COMMITTEE

**Chairperson:** **Mr Frédéric Mallein-Gerin, CNRS, Lyon**

**Experts:**

Mrs Hélène Gautier, Nantes Université (CNU 85)  
Mrs Cécile Legallais, CNRS, Compiègne (CSS7)  
Mrs Danièle Noël, INSERM, Montpellier  
Mrs Stéphanie Ventéo, INSERM, Montpellier (supporting personnel)

## HCÉRES REPRESENTATIVE

Mrs EZINE Sophie

## CHARACTERISATION OF THE UNIT

- Name: Regenerative Nanomedicine
- Acronym: NanoRegMed (RNM)
- Label and number: INSERM\_UNISTRA UMR1260
- Composition of the executive team: Nadia Benkirane-Jessel

## SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement

SVE6 Physiologie et physiopathologie humaine, vieillissement

## THEMES OF THE UNIT.

The UMR 1260 INSERM-UNISTRA (University of Strasbourg) is based on a single team (monoéquipe) entitled 'Regenerative Nanomedicine'. The Unit relies on two themes: Osteoarticular and Dental Regenerative Nanomedicine and Therapeutic Pharmacology and Vascular Regeneration. These two themes focus on three main programs

- (i) Development of active therapeutics and stem cell-based implants for regenerative nanomedicine and bone substitutes;
- (ii) Development of novel therapeutic approaches to regenerate vascular function and organ health;
- (iii) Development of double 3D active implants for neovascularisation to mimic the tumour and to restore organ function.

## HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT.

The UMR 1260 INSERM-UNISTRA was created in January 2018. Until December 2020, the laboratory was spread over three sites (medicine and pharmacy campus). It is now located in a new building, the CRBS (Centre de Recherche en Biomédecine de Strasbourg), in the heart of Strasbourg, bringing together 10 research laboratories and 300 scientists.

## RESEARCH ENVIRONMENT OF THE UNIT.

The Unit is a member of the Strasbourg Federation of Translational Medicine. Several projects are coordinated by the regional transfer of technology structure (SATT Conectus Alsace) and allow the Unit to collaborate with industry. From 2010 to 2019, the Unit was a member of the Labex Medalis. This Labex allowed the Unit to obtain financial support for research against cardiotoxicity of anti-cancer agents. The Unit's basic/preclinical research collaborates with the Reference Center for Oral Manifestations of Rare Diseases, which allows translational research. Several members of the Unit manage hospital services or are involved in patient care, which fosters interactions between research and the clinic and facilitates the transfer from the laboratory to the bedside. The Unit also collaborates with other Units and Institutes in Strasbourg.

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

<b>Permanent personnel in active employment</b>	
Professors and associate professors	22
Lecturer and associate lecturer	10
Senior scientist (Directeur de recherche, DR) and associate	4
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)	5
<b>Subtotal permanent personnel in active employment</b>	<b>45</b>
Non-permanent teacher-researchers, researchers and associates	13
Non-permanent research supporting personnel (PAR)	12
Post-docs	5
PhD Students	31
<b>Subtotal non-permanent personnel</b>	<b>61</b>
<b>Total</b>	<b>106</b>

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

Employer	EC	C	PAR
<b>Université de Strasbourg</b>	30	1	5
Insertm	0	4	0
CNRS	0	3	0
CHU Strasbourg	2	0	0
Others	0	0	0
<b>Total</b>	<b>32</b>	<b>8</b>	<b>5</b>

## UNIT BUDGET

Recurrent budget excluding wage bill allocated by parent institutions (total over 6 years)	<b>673</b>
Own resources obtained from regional calls for projects (total over 6 years of sums obtained from AAP Idex, i-site, CPER, territorial authorities, etc.)	1398
Own resources obtained from national calls for projects (total over 6 years of sums obtained on AAP ONR, PIA, ANR, FRM, INCa, etc.)	3354
Own resources obtained from international call for projects (total over 6 years of sums obtained)	1950
Own resources issued from the valorisation, transfer and industrial collaboration (total over 6 years of sums obtained through contracts, patents, service activities, services, etc.)	2963
<b>Total in euros</b>	<b>7,375</b>

## GLOBAL ASSESSMENT

During the evaluation period, the NanoRegMed Unit has maintained an excellent research production (with an average of 160 publications/year), dedicated to osteoarticular and dental regenerative nanomedicine, therapeutic pharmacology and vascular regeneration, 3D biofabrication and vascularisation for precision medicine. The Unit has strong translational research activities, in line with the previous contract. Significant contributions have highlighted these activities. This is illustrated by the development of a new dressing for cartilage/bone regeneration (Nature Communications) and of a new bone substitute allowing a correct vascularisation and a better graft uptake (Biomedicines); the discovery that PKR2 (ProKineticin-2 Receptor) antagonists could be used to reverse pressure overload and prevent pathological cardiac hypertrophy towards heart failure (Hypertension); the discovery that targeting endothelium-derived microparticles and the angiotensin II type 1 (AT1) receptor represents a new therapeutic approach to delay premature endothelial aging and improve vascular health (Circulation); the development of a tumour model derived from a non-small cell lung cancer patient that can be vascularised (Biomedicines) and an innovative formulation such as a new hydrogel combining hyaluronic acid and extracellular oxygen carrier for the treatment of periodontitis (International Journal of Pharmaceutics). The scientific outputs and activities of NanoRegMed are reflected by a production of high quality (e.g. 2 Nature Communications and 1 New England Journal of Medicine as PI).

There is good visibility of the Unit through the participation of several members, either as invited speaker or chairman in international meetings of the field (between 12 and 15 invitations per year, e.g. IUPHAR World Conference of Natural Products, UK Purine Meeting, Annual Conference of Indian Pharmacology Society, International Association for Dental Research, ...). Participation of clinicians and research directors is high in these meetings.

NanoRegMed has demonstrated an excellent ability to collect large amounts of external resources, mainly at the national level (e.g. 7 ANR grants since 2018, 1 FRM, 2 INCA, Grande Region Est, ...), and at the international level (4 total, with 2 as leader, 1 INCa-MOST grant with Taiwan, 1 ERA-NET).

The exceptional interaction with industry is, without a doubt, one of the main strengths of NanoregMed. It has enabled the unit to obtain 2 million euros in industrial grants, to create 2 start-ups with 12 jobs, to file 6 patents, 3 of which are under license. Its interaction with the non-academic, social or medical world is excellent. The Unit has contributed to recommendations for the management of patients requiring oral care during the COVID-19 epidemic. The Unit contributes to the Pharmacology Education Project developed by The International Union of Basic and Clinical Pharmacology (IUPHAR) as a service to the international pharmacology community and to a larger extent to European Medicines Agency (EMA).

The contribution of NanoRegMed to research training is very active, as evidenced by the many master and doctoral students currently present in the Unit and the number of defended scientific theses (35). The involvement of the members of the Unit in the national teaching programs is important and the international opening must be encouraged. The life and organisation of the Unit are unanimously well appreciated by all members of the Unit. The governance of the director is widely recognised by the members of the Unit and there is unanimous agreement. In total, the Unit has carried out excellent projects, with expertise recognised by the academic community, the industrial world and the medical world.

## DETAILED EVALUATION OF THE UNIT

### A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Clearly, the Unit has considered the recommendations of the previous HCERES evaluation. Indeed, the Unit has improved the following 3 points:

- The Unit has clarified its organisation with 1 team and 3 programs validated by the INSERM and the University and has created an executive committee composed of the director and the topic leaders 'directoire'
- The Unit has also increased its attractiveness. Indeed, researchers have been recruited (4 MCU-PH since 2018 including one in 2021, an Inserm DR2 on mobility in 2019, 2 DR2 CNRS in mobility in 2020, recruitment of 1 PU, 1 PU-PH and 2 MCU on mobility in 2020). However, this does not include recruitment of young full-time researchers and ITA/IATOS as recommended by the previous committee of experts but applications to the national researcher competition and requests for ITA positions were made each year.
- The Unit has increased the number of publications per PhD students and post doc: 16 (including clinical publications) and 5 (excluding clinical publications) publications per student on average during the 2016–2021 period. Engineers and technicians are involved in publications when they contribute to scientific experiments.

The previous committee advised that particular attention should be paid to the collaboration between the different groups in order to make the Unit effective. The late move to the new building did not foster collaboration between the different groups yet. However, since 2021 they are located on the same floor in the new building CRBS and share equipment and expertise. Laboratory meetings are held once a month with all groups where dialogue between researchers and clinicians is easy and appreciated by postdoctoral fellows and PhD students.

### B – EVALUATION AREAS

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

##### Assessment on the unit's resources

The committee assessed that the financial resources are excellent, especially considering the overall fundraising. Concerning the platforms, there is an excellent functioning, and a federative effect on the themes of the Unit. Concerning personnel resources, the evaluation is very good for researchers, postdoctoral fellows, hospital practitioners, but insufficient for technical and administrative staff, despite repeated requests from the Unit Director. The committee evaluates the environment and the premises as very good but which could become excellent if vacant rooms are allocated to the unit after the departure of one PI.

##### Assessment on the scientific objectives of the unit

The scientific objectives have been evaluated as excellent. They are mainly translational and industrial themes, and this guideline seems to be clearly assumed by the members of the Unit. The technological thematic shifts chosen a few years ago are well accepted and the collective reorganisation seems to have been assumed.



## Assessment on the functioning of the unit

The evaluation has shown an excellent global functioning of the Unit at the relational level, and very good at the level of the communication tools. The centralisation of the computerised data still remains to be done together with the development of intranet support and the website refresh.

The management of the Unit seems to be of high quality and appreciated by the different members of the team (researchers, students and ITA). Many common tasks are taken over by the ITAs who ask for a better organisation of their working time. Career development support seems to be well provided and was demonstrated several times during the interviews. Good interactions have been developed between researchers and clinicians. There has been an impact of the move to CRBS and the pandemic on the organisation, but it seems to have stabilised.

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

### Strengths and possibilities linked to the context

The unit is composed of 41 permanent researchers, 14 non-permanent researchers, 2 permanent Unistra technicians, 2 CDD technicians and 35 PhD students. All the members of the lab are committed to carry out and promote preclinical/translational and clinical research.

Members respond successfully to international (5 total, 3 as PI) and European (1 as PI) calls for project: 300 k€ from an ERA-NET project (coordinator), 358k€ from PIA (3 as leader), 2,997 k€ from ANR (11 total, 7 as PI); 1 PHRC n as PI (170k€); Two xInCA as partners; 1400 k€ from 4 local grants as PI, since 2016. These funds are used to purchase major equipment (SEM, FREEZERS, Incubators, electro-spinning equipment...) and to hire approximately 3 PhD students, 10 postdoctoral fellows and 2 engineers per year.

Two start-ups have been created, including, in 2020, Lamina therapeutics, developing innovative combine stem cells and medical devices. A novel biotech company have been developed in collaboration with Institut Curie and Gustave Roussy. Previously, patient-derived tumour xenograft models were developed in nude mice from 2005 to 2017 for kidney, bladder and prostate cancers. This led to the creation of a start-up Urolead in 2010, laureate of the French national competitions for the creation of the innovative business in Emergence category in 2008 and in Creation-Development category in 2010. The laboratory can use these models for its own research.

The laboratory has set up 3 technological platforms which are available to all researchers: TiBioC (Tissue Biofabrication and Characterisation) offers several services, in particular on small- and large-scale 2D and 3D cell models; eBioCyt – UPS1401 was created in 2014 and labelled UPS1401 in 2015 to optimise, enhance and offer technological expertise in cytomics by integrating expertise in ADME/Tox; MicroDyn & cells (Microparticle dynamics and cellular properties) offers the characterisation of extracellular microvesicle. Since 2021, all these activities, with the exception of MicroDyn and the cell platform, have been consolidated in the new CRBS building. Some collaborations have been developed with numerous institutes (Institute of Molecular and Cellular Genetics, Institute of Cellular Biology and Institute of Science and Supramolecular Engineering).

The team is widening with the formulation and bio-pharmacy group arrived since 2021, with expertise in formulation, bio-pharmacy, physicochemical characterisation and functional systems development.

This group is invested in training students and postdoctoral fellows through research.

### Weaknesses and risks linked to the context

Engineers and technicians seem to be a little involved in the publications of the unit.

The creation of start-ups from the laboratory is important. Two researchers are associated with Lamina Therapeutics and one with Ribonexus (each for 20% of their time). Inevitable links of interest must therefore exist to weaken the team spirit.

The associated platforms have very diverse activities and it seems astonishing that they only work with 2 engineers and 2 technicians. This inevitably implies for the functioning of these platforms the involvement of researchers who risk becoming less productive, especially if industrial services are provided. The Unit plans to hire technical staff.

The eBioCyt platform is not located on the site but at the Faculty of Pharmacy and is attached to the University. The operating conditions must be specified, so that it could be as simple as possible for users.

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

Strengths and possibilities linked to the context

The research program concerns tissue engineering, drug delivery, therapeutic discovery, and engineering living materials in order to develop new approaches to improve the quality of life, extend life expectancies, and reducing the overall cost of health care. State-of-the-art-technologies are mentioned such as nanomedicine-smart material, medicinal chemistry-drug discovery, pathway analyses omics, 2D cells and 3D-organoids models, as well as mice models of diseases, and formulations able to target the bioactive molecules or drugs. Many publications attest to this.

A significant part of the activity is dedicated to teaching and training of young scientists, medical and engineers students, with 35 PhD students and 11 Masters 2. During the contract, 91 PhD students (including 19 clinicians) were supervised and 61 have already defended their thesis. Twenty-three have scholarships from foreign countries (Canada, China, Lebanon,). The laboratory has succeeded in producing a portfolio of projects to maintain the balance between emerging projects/consolidated projects/advanced projects, on the one hand, fundamental research/finalised research, on the other hand. Risk-taking is quite important. The transfer of licenses and the creation of companies is particularly developed.

Weaknesses and risks linked to the context

Four main programs are mentioned without any details on how to proceed and the means employed. The distinction between research themes and research programmes is not very clear.

The team is large with 41 permanent members, 14 non-permanent members, but the objectives are broad and there is a risk of not being able to achieve them.

The fact that there is PhD students testify to an intense activity, but the ratio of researchers holding an HDR/PhD is only 1. This implies a significant investment in bench training. The future of doctoral and postdoctoral students could be through jobs in start-ups and other structures created.

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

Strengths and possibilities linked to the context

The laboratory follows the human resource management rules defined by INSERM and Unistra, including gender equality and non-discriminatory. The Laboratory Council is composed equally of women and men. Students of various origins (from Korea, Lebanon, Pakistan, West Africa) are led to the title of doctor with only 4 theses abandoned before defence out of 91 followed in the period.

Over the past 5 years, no major problem has been highlighted (except COVID-19 crisis) and the implementation of health and safety rules has been decreed as the priority of the Unit, with competent referents among the team, and a dedicated internal council. Four prevention assistants have been defined by a framework letter with INSERM and Unistra. These assistants as well as all laboratory managers are made aware of problems relating to occupational health and safety. The Health and Safety regulations of the laboratory, approved by INSERM and Unistra are given to any new temporary or permanent member of the laboratory who must immediately read it and acknowledge receipt and acceptance (signing of the document). A laboratory upgrade campaign has been implemented (display of risk, provision of equipment, tidying up of premises, management of products and waste, good laboratory practices, etc.).

The laboratory is particularly aware of the problems of confidentiality and protection of data. All members of the laboratory undertake upon their arrival to follow the 'internal regulations', and an 'information systems security' charter. When students present sensitive data in the context of written or oral presentations, it is systematically asked to the members of their jury to sign a confidentiality agreement. Access to the unit is authorised (badges) only during the working hours defined in the 'internal regulations'. The opening of a computer account and the allocation of an institutional e-mail address are imperative for this long stay (work station). These accounts are closed when she/he leaves. The use of personal IT resources connected to the institutional network is prohibited.

Twelve members of the team have been trained for animal experiments with conception level with up-to-date skills booklets. For the period, 24 persons were concerned.

## Weaknesses and risks linked to the context

It is very interesting to have appointed 4 prevention assistants to deal with health and safety problems that may arise. Nevertheless, these missions seem to take too much time from their technical activities. These missions should not be done to the detriment of other research, technical or administrative activities. They must not be at the expense of other research, technical or administrative activities carried out. The workload of these assistants must be fully assessed, indicators must be put in place. Audits have been conducted and the results must be shared with the community in order to increase efficiency.

Various commissions (Ethics and Scientific Integrity, Research Strategy, Communication and Seminar Organization, Formation and Pedagogy, Quality Control and Safety, Animal Experimentation) have been set up but the functioning must be specified to the members of the laboratory. There is a lack of commitment to waste management, energy savings (water and electricity) and reducing the carbon footprint.

## EVALUATION AREA 2: ATTRACTIVENESS

### Assessment on the attractiveness of the unit

The committee has evaluated that the attractiveness of the unit is excellent at funding and equipment through platforms and very good at meeting participation and researcher attraction.

Success in funding (ANR, industrial grants, SATT, regional grants) by many researchers in the Unit, either as PI or partner, is excellent. Success for grants for PhD students (MRT, foreign grants) is excellent as well. The follow-up of trained PhD students indicates that 25 are employed in academics or private companies and 17 are postdoctoral fellows or ATER (for known information). The Unit makes available many devices, equipment as well as dedicated expertise through the platforms housed in the Unit and a new equipment (CYFUSE) which is unique in Europe

There is good visibility of the Unit through the participation of several members, either as invited speaker or chairman in prestigious meetings. Participation of clinicians and research directors is high while junior researchers are less represented. During the period, it has to be underlined that the unit has attracted several researchers (3 DR, 1 PU, 1 PU-PH, 6 MCU or MCU-PH) in mobility but no recruitment of researchers with academic positions has been made.

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

## Strengths and possibilities linked to the context

The Unit has organised three international meetings: two symposia ('9<sup>th</sup> international symposium Europe-China on stem cells and regenerative medicine' and Nanomedicine Symposium between Strasbourg and Basel) and the 'International Congress of Bioencapsulation research group of the University of Strasbourg'. The audience is supposed to be mainly national or 'binational'. Several members of the Unit have also taken part to committees for organising international congress (International Symposium on the Mechanisms of Vasodilatation, International Conference on Chemistry & Drug Design) on medical chemistry, cardio-oncology, aging, vascular physiology. Editorial responsibilities are held by several members.

Several Unit members, mainly clinicians but also research directors, are regularly invited to communicate to a large public audience in international meetings (Control Release Society, UK Purine meeting, Symposium Natural Products for Healthy Aging, IUPHAR, ...).

Invitations for communications or session chairs by unit members represent an average of 12-15 per year. They also publish technical articles in journals dedicated to professionals (Ann Intensive Care, Intensive Care, JAMA, Thromb Res, ...). Members are involved in various editorial committees (Journal of oral microbiology, European Journal of Pharmaceutical Research, ...) , in meeting organisations (9<sup>th</sup> International Symposium Europe China on Stem Cells and Regenerative Medicine 2019, NanoMedicine Symposium – University of Basel & Strasbourg 2019, International Conference on Pharmaceutical Chemistry 2016, ...) and belong to international society (European Society of Intensive Care Medicine, International Society on Thrombosis and Haemostasis, ...). This participated to the international visibility of the unit.

## Weaknesses and risks linked to the context

The unit is not very active for evaluating grants from international funding bodies (only one grant evaluation for the Medical Research Council)  
The junior researchers have low international visibility.

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

#### Strengths and possibilities linked to the context

The Unit has trained 89 doctoral students and an average of 10 masters/year over the 2016–2021 period while 10 postdocs have been recruited.

Sixty-one PhD students have already defended their thesis. Twenty-three PhD students were from foreign countries (Korean, Lebanon, West Africa, Pakistan) and had support from the country of origin. Other students received funding through the French government doctoral scholarship, meaning that the Unit is successful to attract fellows and get funding from the doctoral school. PhD students include both scientific and clinicians and the number of publications per student is very high: an average number of publications of 16/students regarding clinicians and an average of 5/students for scientific students. Active collaborations are pursued with the trained junior researchers after going back to their countries. Training is also based on scientific integrity and several rules have been set to sensitise students to transparency, data reliability and reproducibility as well as the management of conflicts of interest.

Attractiveness of the team for junior and senior researchers is indicated by the recruitment and/or mobility of 3 DR, 1 PU, 1 PU-PH, 7 MCU or MCU-PH. This highlights the capacity of the leaders to construct active and powerful relationships on the long term. This is also seen by the hosting of known guest researchers (US, Germany, Japan, Korea, Mexico) for periods going from some days to several months.

The follow-up of the students trained during the period indicates that 15 have been recruited as researcher, MCU or engineers in academics and 3 in hospitals, 2 ATER, 8 as postdocs in France and 7 abroad, 7 in private companies.

## Weaknesses and risks linked to the context

Although PhD students from abroad have been trained in the lab, no fellow from Europe or the US has been attracted.

One weakness is the lack of success to get stable positions for the PhD students or the postdoctoral fellows in academic positions (Inserm, University). The recruitment of young researchers trained in the Unit has failed during the period even though 7 students have competed for stable positions at CNRS, Inserm, University (1 to 3 applications/student).

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

#### Strengths and possibilities linked to the context

The Unit obtained a limited amount of funding from international calls (4 total, 2 as leader INCa-MOST PLBIO with Taiwan, 1 ERA-NET). More national grants were obtained: 3 PIA programs as leader (IdeX, Labex MEDALIS); Twenty-two national grants (11 as coordinator in 4 ANR, 1 PHRC, ...) , other regional sources (8, 4 as leader, in Région Grand Est,..) and foundations and charities (17 total, 5 as coordinator in Fondation Air Liquide, ...) for a total of 1117 k€ for the Unit. The amount of recurring funding from the supervising institutions is 2047 k€. The total budget is 3164k€. This represents an average of 67 k€/employee/5years with a stable position (44 researchers or PH and 3 ITA, excluding non-permanent staff). Independently of the origin of grants, around 60% of funding was obtained by the Unit as coordinator. The budget was allowed to recruit PhD students, postdocs, engineers as well as equipment and consumables.

## Weaknesses and risks linked to the context

The Unit has no EU grant and do not participate to EU networks.

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

##### Strengths and possibilities linked to the context

The Unit is highly attractive via the technical platforms they have created: TibioC, for tissue biofabrication and characterisation of 3D models for normal and tumoral tissues; eBiocyt UPS1401 for innovative 2D/3D coculture cell models and toxicological assay development; MicroDyn&Cell for the characterisation of extracellular vesicles as biomarkers of diseases. The platforms are accessible to public and private laboratories.

A new equipment consisting of a revolutionary 3D tissue-engineering technology has been recently installed thanks to a granted project with Japan CYFUSE technology (550 k€) and is unique in Europe. It is dedicated to the 3D printing of living cells in spheroids/organoids without the need of ink.

##### Weaknesses and risks linked to the context

The technical staff dedicated to platforms is also involved in research activities. The time allowance of engineers to platforms is around 60 to 80%, depending on the platform. Securing the staff who could be devoted full-time to the platform activity is a priority and financial support is expected through fundraising.

### EVALUATION AREA 3: SCIENTIFIC PRODUCTION

#### Assessment on the scientific production of the unit

The overall assessment on scientific production is excellent. The Unit has produced a very high number of publications (904 total) during the contract, well balanced between the scientific (444) and clinical fields (460). The visibility of some of the publications is high (e.g. 1 Nature Communications and 1 New England Journal of Medicine, both as PI).

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

##### Strengths and possibilities linked to the context

The research projects are characteristic of a translational research perfectly feasible thanks to the common presence of researchers and clinicians in the Unit. The clinicians inform about the pathologies affecting the quality of life, the lack of knowledge and treatment, which allows the development of innovative research. The working hypotheses are based on the latest clinical publications in the concerned field. Scientific/medical resources have been developed, such as data banks, cell/tissue banks and cohorts.

From 2016 to 2021, the Unit produced 904 publications among which 428 are signed as first, last or corresponding author. This production was well balanced between scientific (444) and medical journals (460). The production of these publications has been stable over the years with an average of 160 publications/year.

The medical and scientific publications together include a substantial number of papers in high-profile journals, both on the clinical and scientific sides (e.g. Acta Biomateriala, Nanomedicine, Intensive Care Medicine, Nature Communications 1 as PI/5 and New England Journal of Medicine 2 as PI/4).

The high number of papers published in very large audience journals indicates that the Unit's scientific and medical activities result in an original and significant contribution to knowledge at the international level. It also suggests that the objectives of the Unit, to develop innovative translational research, organised in 4 main programs (P), can be achieved based on the success of several products already developed in these categories: (P1) a new wound dressing for cartilage/bone regeneration (Nature Commun 2019 as PI) and a new bone substitute allowing correct vascularisation and improved engraftment (Biomedicines 2021); (P2) novel therapeutic approaches to regenerate/restore cardiovascular and metabolic organ function in diseases (Hypertension 2021, Circulation 2017); (P3) double 3D active implants equipped with well-organized cell organoids for neovascularization to mimic tumor and to restore tissue (Biomedicines 2022); (P4) innovative formulations to improve the biopharmaceutical properties of drugs/use of biomaterials such as polymers, lipids

to conceive original formulations with improved biopharmaceutical characteristics (International Journal of Pharmaceutics 2021). The Unit also has several papers published with international collaborators (USA, Asia, Europe).

### Weaknesses and risks linked to the context

The Unit has a large number of members, with two groups, presented with 4 (or sometimes 3) main programs. Despite the scientific production attests of the quality of its members in their specific areas, expertise does not seem to be shared to result in more original subjects and common publications.

Some research topics are presented to be rather original at the European level, such as the use of nanoparticles for drug targeting, the drug resistance mechanisms in cancer using 2D/3D cell cultures and screening, molecular mechanisms of periodontitis, ... but a number of European laboratories already work on these topics.

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

### Strengths and possibilities linked to the context

The high number of papers (around 50) published in high-profile journals as PI attests that the Unit does not compromise research quality to quantity. The topics of the journals are generally translational/clinical research-oriented and reflect the involvement and level of expertise of both scientific and clinician members. The Unit is one team with 4 programs of research and the production of these 4 programs is evenly distributed between the programs.

All the permanent and non-permanent members of the Unit seem to contribute to the scientific production, including researchers, teacher-researchers, clinicians, students, and postdoctoral fellows. Most of the postdocs and PhD students have published at least once as first author and are co-author in several publications. The average number of publications by PhD students (excluding clinicians) is 5.

There are a significant number of editions of chapters of books in the medical field with also 4 directions of scientific books and 14 chapters of scientific works.

### Weaknesses and risks linked to the context

The number of technical and administrative staff members is limited (2 for 41 permanent members, 10 postdocs, 35 PhDs), which may slow down the progression of the work. The scientific work of the technical staff is greatly diminished by multiple menial tasks that are asked to them without warning on a daily basis.

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

### Strengths and possibilities linked to the context

The Unit takes scientific integrity and the transmission of good research practices to all members seriously. The researchers comply to the French National Charter for Research Integrity, the data are recorded in a lab notebook or in electronic files that are the property of the lab. The Unit is helped in this aspect of good practice of scientific integrity by a member of the Unit who is Member of the Ethical Committee for Research of the University of Strasbourg (CER Unistra). In addition, doctoral students are trained in scientific integrity and research ethics by their doctoral school and benefit from a newcomer day with sessions devoted to good laboratory practices.

The Unit also ensures that clinical and animal studies comply with current legislation. Projects including work on animals or human resources are submitted beforehand to the standard French ethics committees (CPP, Centre de Ressources Biologiques, PHRC) for validation.

Researchers are encouraged to publish their articles in open access. During the contract, this policy has resulted in more than 50% of publications in open access. Moreover, the final versions of the papers not published in open access are registered in HAL. The research data are stored on computers and external disks to ensure their backup.

### Weaknesses and risks linked to the context

The researchers save their data individually, on external hard drives. There is no centralised backup of scientific data generated in the Unit (no central server), which constitutes a significant risk of loss of work, a lack of traceability, a lack of management control over all scientific production, and a difficulty in sharing data within the Unit.

## EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

Overall, the Unit shows an excellent contribution of research activities to society. It shows an outstanding activity of industrial collaborations, with 6 new patents and 3 licences and the creation of 2 start-ups. The concrete application of research activities in regenerative medicine is excellent with a phase I/II clinical trial scheduled for 2023 by the start-up Lamina Therapeutics. This is a promising breakthrough innovation that could open up new therapeutic avenues in the field of bone and cartilage regeneration to treat osteoarthritis, which affects several hundred million people worldwide.

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

#### Strengths and possibilities linked to the context

The Unit has long time experience of valorisation and this is an ongoing strength of the Unit, with 6 new patents, among which 3 are licenced, and with the creation of 2 start-ups during the contract, Lamina Therapeutics (for the treatment of osteochondral lesions of the knee) and Ribonexus (anti-cancer therapy based on mRNA control). Lamina therapeutics was strongly supported by the SATT Conectus from the University of Strasbourg at the beginning of its creation. Other contracts involve companies specialised in dentistry (medical devices, oral implants).

The Unit has 2 ways of interacting with industrial partners: by providing technical services through its platforms or by collaborating with partners, extending its own scientific interests (e.g. development of new prognostic markers). The selection of partners is based on the interest and expertise of the Unit. For instance, the projects developed with non-academic partners concern new medical devices for cartilage/bone reconstruction and treatments of vascular dysfunctions, all of which are major societal challenges.

Collaborations with industrial partners allow the unit to work on specific research themes with important medical implications, such as the development of implants for the elderly, or for people with metabolic or genetic diseases. The Unit also benefits from the experience of industrial partners to build clinical trials or to better stratify patient cohorts like with Diagnostica Stago, a world leader in the science of haemostasis and thrombosis. These collaborations allow the Unit to develop personalised medicine in the case of cancers where patient tumours are recreated to screen and select therapeutic molecules before administration (collaborations with Transgene and CYFUSE).

The Unit hosts 2 start-ups and several doctoral students and postdocs are financed by non-academic partners. Clinicians and Professors of the Unit give learning sessions at the University of Strasbourg to teach recent advances in scientific knowledge but also to industrial partners, including big pharmaceutical companies. The Unit benefits from economic returns from its technology transfer to industry through team contracts and in the form of individual expertise for 6 members of the Unit who dedicate 10 to 20% of their time to consulting.

The members of the Unit participate in the popularisation of science in society (Better food for better life) are present in patient associations (Dysplasies ectodermiques).

#### Weaknesses and risks linked to the context

It is said that several PhD students are financed by non-academic partners and there are a large number of industries collaborating with the Unit but there has been a low number of CIFRE PhDs obtained during the contract (1 finished and 3 ongoing).

The nature of the 'partnerships' between the Unit and certain pharmaceutical companies regarding cancer treatment is not yet stabilised (e.g. Astra Zeneca grant under evaluation, European Innovation Council challenges and call for Recherche Hospitalo-Universitaire-RHU under submission).

The confidential aspect of seminars shared at the Unit level and which mix academic members with different industrial partners is not documented.

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

### Strengths and possibilities linked to the context

There is a strong activity of valorisation of the Unit with the creation of start-ups with 12 jobs and the filling of 6 patents.

The Unit has contributed to recommendations for the management of patients requiring oral care during the decontamination period during the COVID-19 epidemic. These recommendations have been published in the health care guides.

The Unit contributes to the Pharmacology Education Project developed by The International Union of Basic and Clinical Pharmacology (IUPHAR) as a service to the international pharmacology community and to a larger extent to European Medicines Agency (EMA).

### Weaknesses and risks linked to the context

No particular weakness.

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

### Strengths and possibilities linked to the context

The Unit participates in popularisation conferences during various national days dedicated to citizen-researcher meetings on public sites or in associations. The Unit disseminates its activity through social media (LinkedIn) and through an international Master of Biomedicine at the University of Strasbourg.

The researchers publish articles in journals for the general public and in journals specialised in biotechnology, pharmacology and medicine. They speak at public conferences to share their research on rare diseases.

The Unit also helped share knowledge and advances on COVID-19 during the pandemic, or on diabetes and osteoarthritis, for example, through radio and television interviews.

The Unit welcomes regularly third-grade trainees.

### Weaknesses and risks linked to the context

Given the large number of members in the Unit, participation in social events with direct contact with citizens could be more important. Only some leaders seem to participate in media outreach events.

## C - RECOMMENDATIONS TO THE UNIT

### Recommendations regarding the Evaluation Area 1: Profile, resources and organisation of the unit

As both start-ups seem to be successful, an effort can be made to negotiate research contracts allowing a better financial return for the laboratory. Also, part of the funding from industrial contracts (45% of total funding) with the platforms could be allocated to the development of ambitious internal collaborative projects.

Regarding the prospective dimension of its policy, the Unit must ensure that it maintains quality basic research to feed its translational research.

As far as its personnel is concerned, too many common tasks are taken care of by a too limited number of technicians. A policy of recruiting fixed-term contracts must be undertaken when contracts are requested.

The work organisation chart of the Unit must be clarified by specifying the functions of the persons in charge. Likewise, the missions of the different commissions need an action plan, with precise tasks, visible to all.

As far as the life of the Unit is concerned, a day or a retreat of the Unit could be the occasion for presentations not only scientific but also technological, an occasion also to highlight the technical staff and to assure them recognition. This recognition could be improved by including them more in publications.

Care should be taken to disseminate conference announcements more widely among younger researchers (including PhD students).

It is important to set up tools for sharing information (IT resources, intranet) and for saving data.



## Recommendations regarding the Evaluation Area 2: Attractiveness

A third of the meetings organised have been by a member who is an outgoing researcher and such activity has to be pursued by other team members to maintain the visibility of research expertise and keep open new opportunities for collaborations. Young researchers need to participate more in conferences.

The average number of defended PhD students/HDR is 1 for the contract period (35 PhD/36 HDR), which could be increased to stimulate research activity and publications.

The unit should apply to more international calls, since international research funding (such as those proposed by the ANR or the EU) are very attractive for high-quality and motivated trainees. PhD funding might be increased from other sources: national research programs, foundations... Only 1 CIFRE thesis was obtained during the contract, 3 after, and this effort of obtaining CIFRE must be continued considering the strong industrial environment of the Unit

The Unit has not been successful in recruiting its PhD students or postdocs to academic positions. Strategies for training non-tenured researchers to improve their CVs and submission packages could be undertaken. In parallel, the Unit must adopt a strong strategy to attract young PIs to compensate for the departure of current senior researchers.

The Unit must maintain its efforts to respond to European and international calls for proposals. Increased funding through these channels would guarantee the budget for students and postdocs as well as for equipment and consumables for several years.

The securing of engineers working on technological platforms through stable positions could be stimulated by service offers and publicity at regional and national levels through a website, participation in conferences, LinkedIn-type networks...

## Recommendations regarding Evaluation Area 3: Scientific Production

The Unit is encouraged to maintain the production of its scientific activity in balance with its clinical production. The unit should take advantage of the multiple and varied expertise that exists internally to develop innovative and interdisciplinary high-level research projects, which should result in an increase in the number of high-level scientific publications.

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

The young researchers should be more involved in the disseminating activities regarding the technological and scientific achievements.

## CONDUCT OF THE INTERVIEWS

### Date(s)

**Start:** 12 octobre 2022 à 9 h

**End:** 12 octobre 2022 à 18 h

**Interview conducted: online**

### INTERVIEW SCHEDULE

8 a.m.-9 a.m. Réunion du comité (huis clos)

9 a.m. Presentation of the committee

9:15 a.m.-10:30 a.m. Highlights of the Unit by the Director and main results presentation

Coffee break

10:45 a.m.-12 p.m. Committee debriefing

12H00-13H00 LUNCH

1:15 p.m.-1:45 p.m. Meeting with technicians and administrative staff (closed doors)

1:45 p.m.-2:15 p.m. Meeting with PhDs and postdocs (closed doors)

2:15 p.m.-2:45 p.m. Meeting with researchers (closed doors)

Coffee break

3 p.m. – 3:30 p.m. Meeting with the representatives of the local institutions

Université de Strasbourg :

La déléguée santé Valérie Lamour

Inserm

La déléguée régionale adjointe : Ana Lazar

L'adjointe au président de l'ITMO technologie pour la santé : Marie-Josèphe Leroy-Zamia

Coffee break

4 p.m.-4:30 p.m. Closed-door meeting of the committee

4:30 p.m.-5 p.m. Meeting with the Director

5 p.m.-6 p.m. Committee meeting (closed doors)

### PARTICULAR POINT TO BE MENTIONNED

## GENERAL OBSERVATIONS OF THE SUPERVISORS

**Université**

**de Strasbourg**

Monsieur Éric Saint-Aman  
Directeur du Département d'évaluation de la recherche  
HCERES - Haut conseil de l'évaluation de la recherche et  
de l'enseignement supérieur  
2 rue Albert Einstein  
75013 PARIS

Strasbourg, le 11 mai 2023

Objet : Rapport d'évaluation DER-PUR230023320 - NanoRegMed - Nanomédecine régénérative

Réf. : RB/FF/ 2023-200

**Rémi Barillon**

Vice-Président Recherche,  
Formation Doctorale et Science  
Ouverte

Cher Collègue,

**Affaire suivie par :**

Florian Fritsch  
Responsable du département  
Administration de la recherche et  
accompagnement des chercheurs  
Tél : 03.68.85.15.19

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L'université de Strasbourg vous remercie ainsi que tous les membres du comité HCERES pour le travail d'expertise réalisé sur l'unité de recherche «Nanomédecine régénérative» (NanoRegMed - UMR\_S 1260).

Vous trouverez ci-joint les observations formulées dans le cadre de ce rapport.

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

Rémi Barillon

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**Objet : Observations suite au rapport d'évaluation DER-PUR230023320 - NanoRegMed**

Concerning the following sentence (page 8, "Assessment on the unit's resources"):  
*"The committee evaluates the environment and the premises as very good but which could become excellent if vacant rooms are allocated to the unit (...)"*

- The surface allocation will depend on the future affiliation of the PI of the departing group and it cannot be assumed at this stage that additional space will become available to this research unit. This will be a decision of the governing bodies, University of Strasbourg together with Inserm taking into account the other research units in the CRBS building.

Concerning the following paragraph (page 18, "Responses to supervising bodies concerns (if any)" ) :  
*"The place of the UMS within CRBS needs to be clarified, in terms of its relationship with the Unit. In particular, the effort must be put on the positioning of the technical and administrative staff (...)."*

- After two years of experimentation of a new type of UMS, an evaluation of the implemented processes is in progress to optimize its efficiency for the benefit of all the research units hosted in the CRBS building.

The Hcéres' evaluation reports are available online:  
[www.hceres.fr](http://www.hceres.fr)

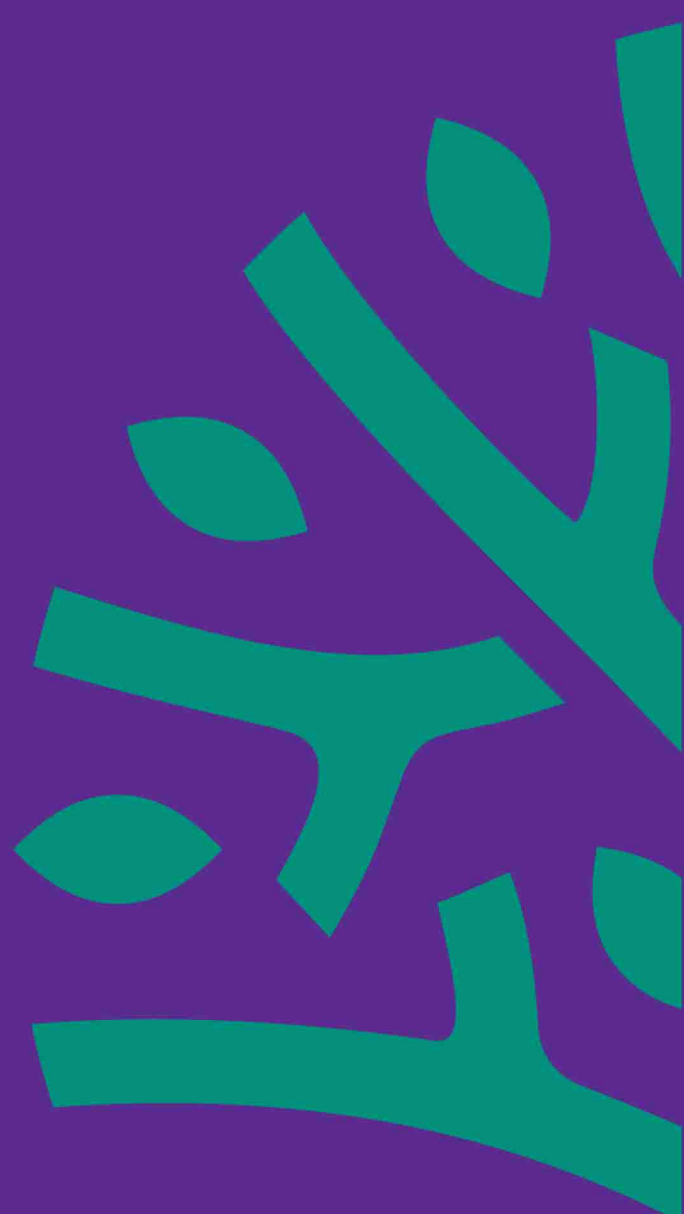
**Evaluation of Universities and Schools**

**Evaluation of research units**

**Evaluation of the academic formations**

**Evaluation of the national research organisms**

**Evaluation and International accreditation**



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