



Research evaluation

EVALUATION REPORT OF THE UNIT
SIMPA - Stress, IMmunity, PAt pathogens

UNDER THE SUPERVISION OF THE
FOLLOWING ESTABLISHMENTS AND
ORGANISMS:

Université de Lorraine

EVALUATION CAMPAIGN 2022-2023
GROUP C

Report published on June, 01 2023

High Council for evaluation of research and higher education



In the name of the expert committee¹ :

Peter Van Endert, Chairman of the committee

For the Hcéres² :

Thierry Coulhon, President

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

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

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

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

MEMBERS OF THE EXPERT COMMITTEE

Chairperson: Mr Peter Van Endert, Université Paris-Cité

Experts: Ms Vassilia Bayle Theodorou, École d'Ingénieurs de Purpan
Mr Stéphane Fontanay, Université Claude Bernard Lyon 1 (supporting personnel)
Mr Christophe Lefebvre, Université de Lille (representative of CNU)

HCÉRES REPRESENTATIVE

Ms Muriel Mercier-Bonin

CHARACTERISATION OF THE UNIT

- Name : Stress, IMMunity, PATHogens
- Acronym: SIMPA
- Label and number: UR 7300
- Composition of the executive team: Mr Jean-Pol Fripiat

SCIENTIFIC PANELS OF THE UNIT

SVE: Life, health and environmental sciences

Panels by descending order of importance as indicated by the unit:

SVE4: Immunity, infection and immunotherapy

SVE5: Neurosciences and nervous system disorders

ST3: Earth and universe science

SVE7: Prevention, diagnosis and treatment of human diseases

THEMES OF THE UNIT

SIMPA (UR 7300) is a single-team research unit originally formed by grouping a young team headed by the present director with microbiologists from another team and one neurologist. The neurobiology component of the unit has been strongly enhanced at the beginning of 2022 by the joining of four neurobiologists. Consistent with this staff composition, the overarching topic studied by unit's scientists relates to the effect of chronic gravitational and mild socio-environmental stresses on the immune and nervous systems as well as on gut microbiota. In this context the unit has the ambition that its research not only informs on health risks in future space missions but also is of interest for understanding and dealing with omnipresent societal stress.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

UR 7300 is located on the Biology & Health Campus of the Université de Lorraine in Nancy and one of the ten research and support units forming the "Pôle" Biology, Medicine, and Health" (BMS) on this campus. While UR 7300 has dedicated space for all its members, the last five years saw the renovation of its laboratory space, which lasted 2 years and 7 months and dispersed its members to three different locations. All gravitational experiments conducted by members of the unit are now performed at the GEPAM (Gravitational Experimental Platform) platform, which was created in 2019 and to which UR 7300 equipment useful for gravitational experiments was moved. The unit has also access to a core facility (Ingénierie, Biologie, Santé en Lorraine - IBSLor) where sequencing, flow cytometry and other experiments requiring large equipment are performed.

RESEARCH ENVIRONMENT OF THE UNIT

UR 7300 is involved in multiple research initiatives and structures at the local, regional, national and international levels.

At the level of the BMS campus, interactions exist with two INSERM (UMR7365, S1116), one CNRS (UMR7274) and one service (USC INRAE 340) units. One of these (UMR7274) has given rise to two publications.

UR 7300 also participates in projects and programs of its university, in the context of a State-Region contract and an excellence initiative (IMPACT Biomolécules). Furthermore, it benefits from a regional Research Cooperation Fund (3BR). Each of the latter participations results in financial contributions to the unit's budget.

UR 7300 interactions at the national and European levels are predominantly based on the unit's work related to space flight. UR 7300 has a partnership with the National Centre for Space Studies (CNES) and with the Belgian Nuclear Research Centre. Numerous links exist with the European Space Agency (ESA). Thus UR 7300 is participating in eight projects funded by ESA three of which it coordinates. UR 7300 moreover participates in three ESA topical teams on varied subjects from Immunity in Space to Advanced Compound Microscopy or Developmental Biology in Vertebrates; how the two latter link to UR 7300 research is not clearly assessed. Finally, UR 7300 contributes to roadmaps for ESA and two roadmaps for the International Space Station (ISS), and its director is member of a Life science advisory group for ESA. Clearly links with ESA are pivotal for UR 7300 identity and activity.

Next to ESA and CNES links, UR 7300 also interacts with a laboratory at the LMU (Ludwig-Maximilian University) in Munich interested in stress and immunity, and with an Institute of Biomedical Problems in Moscow.

9 out of 16 scientists have hospital activities taking care of hospital laboratories, patients with neurological disorders or "medical specialties", also assuming various leadership responsibilities. In the context of these activities, they participate in medical research that has given rise to 95 publications over the report period.

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

Permanent personnel in active employment	
Professors and associate professors	6
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)	6
Subtotal permanent personnel in active employment	18
Non-permanent teacher-researchers, researchers and associates	2
Non-permanent research supporting personnel (PAR)	0
Post-docs	0
PhD Students	5
Subtotal non-permanent personnel	7
Total	25

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

Employer	EC	C	PAR
Université de Lorraine	12	0	6
Université Paris Descartes	0	0	0
Université de Rouen Normandie	0	0	0
Total	12	0	6

UNIT BUDGET

Recurrent budget excluding wage bill allocated by parent institutions (total over 6 years)	242.638
Own resources obtained from regional calls for projects (total over 6 years of sums obtained from AAP index, i-site, CPER, territorial authorities, etc.)	222.620
Own resources obtained from national calls for projects (total over 6 years of sums obtained on AAP ONR, PIA, ANR, FRM, INCa, etc.)	244.800
Own resources obtained from international call for projects (total over 6 years of sums obtained)	123.010

Own resources issued from the valorisation, transfer and industrial collaboration (total over 6 years of sums obtained through contracts, patents, service activities, services, etc.)	112.395
Total in euros (€)	945.463

GLOBAL ASSESSMENT

UR 7300 SIMPA (Stress, IMMunity, PATHogens) is a single-team research unit located on the Biology & Health campus of the University of Lorraine in Nancy. UR 7300 is one of ten research and service units grouped in the Biology, Medicine and Health pole. The principal topic studied by UR 7300 concerns the impact of stress experienced during space flight on the immune system with focus on B lymphocytes, on microbiota and on the nervous system. The unit has the ambition to extend this topic to the study of chronic societal and environmental stress, based on the assumption that microgravity and societal stress have similar impact on health.

The overall resources of the unit, which is composed exclusively of university lecturer-scientists and clinicians, are excellent. The unit collaborates with local, national and international teams and has access to state-of-the-art core facilities. The scientific objectives of the unit centred on gravitational stress are original and the unit could consider applying for recognition as rare discipline by the university. The unit benefits from strong national and international recognition through permanent collaboration with the National Centre for Space Studies (CNES) and particularly through coordination and participation of projects funded by the European Space Agency (ESA). The unit also maintains productive collaborations with teams in Belgium, Germany and Russia. Thus, the visibility and attractiveness of the unit are excellent.

The scientific production of the unit has globally been excellent, although mechanistic studies remain to be reinforced. The unit publishes both in speciality and in "generalist" (*FASEB J.*, *Scientific Reports*) journals. During the last years the unit has established the CUMS (Chronic Unpredictable Mild Stress) model and set-up a new Gravitational Experimental Platform (GEPAM) which has been integrated in the range of ground-based ESA facilities and is open for use by academic and non-academic partners. To develop use of this platform by both types of partners, attribution of a dedicated engineer would be desirable.

The committee anticipates that the availability of the CUMS model and GEPAM platform will facilitate the development of mechanistic studies. Moreover, the CUMS model could be instrumental for studying stress experienced during space flight without access to samples from actual personnel of space missions. However, exploring the physiopathology of chronic ground level stress through models designed to mimic space flight remains a conceptual and experimental challenge and could be one important focus of UR 7300 research in the coming years. As the unit has been or will shortly be joined by four neurobiologists, integration of immunological, microbiological and neurobiological approaches to the study of gravitational and chronic societal stress should be another focus of research in the coming years.

UR 7300 has established collaboration with private companies, for example resulting in common supervision of PhD students (Cifre funding). However, results of interest for protection of intellectual property have not been obtained. UR 7300 also is active in conveying issues of space-related research to the public. Thus, the overall contribution to society is very good.

UR 7300 is in a transition period, with both the director and the composition of the unit changing. As the current director played a key role not only in the recognition of the unit but also in its research focus and its internal functioning and cohesion, unit management should work to implicate all unit personnel actively in the transition. Moreover, the arrival of four neurobiologists will necessarily affect the focus of unit's research underlining the importance of implicating all unit's staff in defining research objectives and policy.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

(The team should consider improvement of its publication strategy.

More cross- and interdisciplinary publications should be encouraged.

The team should continue addressing underlying mechanisms, despite the operational and technical constraints and limitations of challenging space flight experiments.)

Publishing in top-ranked journals is considered difficult for work in the scientific domain according to UR 7300, thus this could not be achieved. Planned broadening of research to chronic socio-environmental stress may help to increase interest for UR 7300 research and therefore its impact, however this remains to be achieved.

UR 7300 has increased the number of interdisciplinary publications, 16 papers corresponding to 34% of scientific (non-clinical) publications were interdisciplinary.

UR 7300 plans that availability of the GEPAM platform will facilitate undertaking mechanistic studies previously wanting in UR 7300 research.

(The expert committee recommends widening the scope of the EA7300's work to a societal interest and to develop and strengthen the rationale of the possible health/social/economic benefits.)

Although the availability of the CUMS model and the setup of the GEPAM platform allowed for addressing this issue, the splitting of the unit during renovation works and the sanitary crisis did not allow to make marked progress yet.

(Strengthening the research projects in chronic socio-environmental stresses will further improve the interaction with the social, economic and cultural environment.

The committee recommends to more generally strengthening interactions with the environment (companies, local and public authorities, general public)

UR 7300 has secured new funding from one private company and from two regional public sources.

(In addition to the unit's objective to use common funds to invite one or two external speakers each year, the set-up of a journal club in English may be an easy way to stimulate and sustain a more general scientific interest.)

A journal club in English language is now implemented once a month. The additional suggestion to invite one or two external speakers each year could not be implemented during the sanitary crisis.

(The important international collaborations of the unit should allow attracting more foreign post-doctoral fellows, possibly through existing collaborations or by participating in international training programmes.)

The suggestion to attract (more) postdoctoral researchers could not be implemented. This is ascribed partly to the difficult situation of a split lab during renovation work, as well as to the withdrawal of one candidate who had been selected for a CNES fellowship.

(Most equipment was acquired before 2011.)

The unit has acquired new equipment or renewed equipment for the amount of 326 k€.

(7 out of 12 permanent professors and assistant professors are engaged in clinical practices. There is an immanent risk of an unbalance between fundamental and clinical research in a context where all other permanent professors and assistant professors belong to the university and have a heavy charge of teaching. A scientific staff composed only of lecturer-researchers entails a risk in a highly competitive scientific community.)

UR 7300 unsuccessfully requested repeatedly an additional lecturer position; but obtained two technical assistant positions (Biatss). Also, four neurobiologists joined the unit in 2022. Thus, the global workforce is significantly enhanced and to some extent reoriented to a stronger neurobiology component.

(The three main axes are interesting and to be developed, but the size of the team requires to focus on the one or two main axes which are the most promising, e.g. to further dissect the CRH receptors in B lymphocytes in terms of epigenetic regulation, activating pathways and consequences of their inhibition on the adaptive response in the intimacy of the gut microbiota.

The unit contends that the addition of two Biatss and five lecturer-scientists increases the workforce of the unit and therefore its capacity to study multiple lines of research.

Recent literature has shown the direct role of the intestinal microbiota on bone development and structure. It may be interesting to also look at this parameter in the stressed mouse model, as it might contribute to the impact of stress on B cell lymphopoiesis.

This suggestion is considered interesting by the unit but could not be implemented due to construction work and local separation of unit's scientists.

As part of a global objective to provide a larger societal interest, it may be interesting to develop in vivo (mouse) models to further address the functional impact of immune modifications induced under stress conditions on host health.

The unit has responded to this recommendation.

Because of the major role of the commensal microbiota on maturation of intestinal B cells and of the importance of the gut-brain axis, characterization of CRH receptor expression and its role on B cells from the intestinal compartment may complete the work on the peripheral compartment.

Implementing this suggestion was also hampered by construction work and separation of unit scientists.

For achieving the ambitious goals and success of the research program, the projects need to follow consequently a precise line of main questions and objectives, to define and review continuously priorities, and to focus on major important mechanisms and on functional studies.)

The unit points out projects concerning the role of the methyl transferase EZH2 in the effect of microgravity on thymopoiesis, and its participation in the ESA projects Flumias and IncRNA.

B - EVALUATION AREAS

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

Assessment on the unit's resources

The overall resources of the unit are excellent. Due to their original themes of research, they have applied and have been awarded by several grants of the European Space Agency.

Assessment on the scientific objectives of the unit

The scientific objectives of the unit are focused on stress and immunity associated with spaceflight. This is a very peculiar and original topic in the landscape of French research and was qualified as excellent.

Assessment on the functioning of the unit

The functioning of the unit complies with all safety rules, involves the participation of the staff and was considered as excellent by the committee.

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

Strengths and possibilities linked to the context

The unit participates in University of Lorraine's major projects; this includes the Bioengineering for Health project under the CPER (Contrat de Plan État Région) and the 'IMPACT Biomolécules' project, part of the University's I-SITE (Initiatives Science-Innovation-Territoire- Économie) resulting in significant funding: 85 k€ of equipment, 78 k€ of consumables and 139 k€ of salary.

The unit has enlarged its funding sources through industrial R&D contracts with the companies SEPTEOS SAS and AVRIL.

The building hosting the laboratory has been renovated during the present contract and the unit has invested own resources of 326 k€ to complete its equipment.

The creation of the original GEPAM has been a hallmark of the present contract. This facility has been integrated into the ESA ground-based facilities portfolio in March 2020.

The unit benefits from renovated premises and acquisition of new equipment funded by own resources. As member of the Lorraine University's BMS pole it takes advantage for interdisciplinary collaborations, access to

platforms and participation in projects. The members of the unit, including Biatss, are strongly involved in teaching. Moreover, many members are part of the CHRU of Nancy, which increases the possibilities of interdisciplinary collaborations.

The unit participates in European projects mainly by applying to ESA projects that fit well their scientific activities. As such they were granted with 3 ESA projects as leaders and five as partners over the reporting period.

The unit has increased its human resources; two Biatss with a permanent position (one Assistant Engineer and one technical assistant) and one MCU-PH have integrated the unit during the present contract. Furthermore four neurobiologists (two PU, one MCU and one MCU-PH) have joined UR 7300 at the beginning of 2022.

Weaknesses and risks linked to the context

The exclusive composition of the scientific unit's staff by lecturer-researchers with heavy teaching duties, and hospital physician-scientists with substantial clinical and teaching tasks, limits the capacity of the unit to carry out ambitious research projects.

The decrease of the recurrent CNES grant curtails the financial resources of the unit.

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

Strengths and possibilities linked to the context

The unit has a national and international reputation and visibility in the field of stresses and immunity associated with spaceflight highly recognized by ESA, as attested by success in multiple ESA project calls.

The scientific objectives are original, dealing with the risk assessment for future long-duration space missions but also providing knowledge for chronic socio-environmental stresses impact on immunity and microbiota. The animal models of gravitational stress, CUMS (Chronic Unpredictable Mild Stress) are excellent.

The unit has good knowledge of international competitors and collaborates with them through the ESA projects, e.g. the Belgian nuclear research centre (Mol) and the Institute of Biomedical Problems (Moscow).

The research theme of the unit is in line with the project of the BMS (Biology, Medicine and Health) campus to study healthy and pathological aging. This is because pathophysiological perturbations that manifest in healthy humans during their adaptation to space have all the characteristics of accelerated aging. This link to the BMS mission attracts support for UR 7300 research by the supervisory body (University of Lorraine).

Participative scientific policy decisions in UR 7300 are facilitated by the single-team composition and the management system adopted; the laboratory board fixing the scientific strategy is composed by 14 of 16 permanent team members and two PhD students.

Emerging projects proposed by young lecturer-scientists can receive financial support from a 10% levy on all unit contracts after selection by the unit's board.

The research performed by the unit aims to have a socio-economic impact through (i) transposition of the stress/immunity/microbiota findings obtained in spaceflight-mimicking conditions to everyday life chronic socio-environmental stresses and (ii) industrial collaborations for preventive/curative treatments by antioxidants as well as antifungals; the latter have resulted in 2 Cifre grants with the companies AVRIL and SEPTEOS SAS.

Weaknesses and risks linked to the context

Projects aiming to deepening the mechanism of the dialogue between the microbiota and the nervous and immune systems have little been developed and have a low number of publications.

The mechanistic approaches are not deepened enough.

A link between basic research carried out in UR 7300 and clinical investigations by its physician-scientists is not readily evident.

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 unit's management system is participative (bureau and laboratory board, exchanges with all members during assemblies).

The sex ratio of unit's staff is slightly improved for the present contract, with 16 women (67%) and 8 men (33%) versus 14 women (70%) and 6 men (30%) for the previous contract.

Two Biatss were recruited between 2019 and 2021; one promotion was obtained in 2020 and one technician gained a permanent position in 2020.

Permanent and non-permanent members have access to training courses.

Unit's functioning complies with safety rules. Two prevention assistants maintain the 'health and safety at work' register up to date and update the risk assessment document, which is then sent to University's health and safety managers. The unit's members are informed and trained with respect to occupational hazards. The prevention assistants regularly follow training courses given by the University.

Three permanent members are trained for prevention of psychosocial risks, including sexual harassment.

The unit has access to appropriate storage modalities of research data (PETA service of University of Lorraine).

The BCP (business continuity plan) is regularly updated.

UR 7300 has undertaken some actions for awareness to sustainable development goals, e.g. reducing carbon footprint by virtual meetings.

Weaknesses and risks linked to the context

Although some sustainable development measures (e.g. limitation of air travel, online meetings) are described but their impact has not been quantified.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

Members of the unit have been invited to international meetings, they have contributed to the organization of several international congresses and are members of editorial boards.
The overall attractiveness of the unit is excellent with respect to its international and national recognition.

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 members of UR 7300 have been invited to give 11 lectures abroad in academic institutions or at international and European congresses (Annual Meeting of the International Society for Gravitational Physiology). They also contributed to the organization of national/international congresses (e.g. Annual Congress of the French Society of Microbiology, Annual Meeting of the International Society for Gravitational Physiology).

The members of UR 7300 are fully involved in Editorial boards (*American Journal of Experimental and Clinical Research, Psychopharmacology, Frontiers in Physiology section Environmental, Aviation and Space Physiology, Journal of Medical Mycology, Open Journal of Molecular and Integrative Physiology, Scientific Reports, International Journal of Molecular Sciences*).

The members of UR 7300 take part in ESA topical teams: 'Developmental Biology in Vertebrates', 'Stress Challenges and Immunity in Space' and 'Advanced Compound Microscopy, from Molecules to Organism morphology' and in the development of roadmaps for ESA (2016-2020) and for International Space Station ISS (2024-2030). They take part in the 'Life Sciences Advisory Group' of ESA. Their GEPAM platform was qualified as ESA portfolio of ground-based facilities.

The UR 7300 scientists are members of multiple CNU (sections 45.01 (bacteriology-virology), 57-01 (periodontology), 58-01 (Restorative dentistry, endodontics, prosthetics, function-dysfunction, imaging, biomaterials)). They take part in Hcéres committees, in grant expertises (Agence Nationale de la Recherche ANR, Association nationale de la recherche et de la technologie ANRT, Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail ANSES, Centre National de la Recherche Scientifique CNRS, and international organisations, e.g. Fonds de Recherche Scientifique de Belgique Francophone, Netherlands Organization for Scientific Research, Czech Science Foundation) and in more than 100 reviews of publications (e.g. *Faseb J*, *NPG microgravity*, *Scientific Reports*).

The scientists of UR 7300 are members of learned societies (Committee on Space Research COSPAR, European Low Gravity Research Association ELGRA, International Society for Gravitational Physiology ISGP, French Society of Microbiology etc.) and were awarded with clinical research or basic research prizes (Meridol prize, Sunstar prize).

Weaknesses and risks linked to the context

None.

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

Strengths and possibilities linked to the context

The members of UR 7300 perform more advanced experimentation on the platforms of the IBSL or UMS 2008/US40 service unit or through engaging in collaborations with other units of the BMS pole.

The new laboratory located centrally in the medical faculty and close to other BMS laboratories, as well as the opening of the GEPAM platform, will increase opportunities to attract renowned guest researchers in the coming years.

Scientific meetings are held every two weeks, dedicated to presenting experimental results or bibliography during journal clubs, which are given in English once a month.

UR 7300 has trained 13 PhD students (5 on-going) during the reporting period.

UR 7300 has created a PhD monitoring committee in accordance with the local BioSE (Biologie Santé Environnement) Doctoral School to promote oral presentations at a research day every year as well as a strategy to promote the participation of PhD students in national or international conferences.

UR 7300 initiated the recruitment of a young MCU-PH and neurobiologists to boost the field of neuroinflammation in the laboratory.

UR 7300 set up internal rules to (i) support emerging projects led by junior researchers in line with the unit's theme through a 10% levy on contracts, (ii) give priority to new researchers for applications to the annual University call (Support for Research Actions) and (iii) favour ethics training (scientific integrity and open science policy).

Weaknesses and risks linked to the context

The renovation work of the unit's buildings took a long time (2 years and 7 months instead of one year as initially planned), which created difficult working conditions by separating equipment and staff on three different sites during this period, although this also promoted new local interactions with other research units.

There was no post-doctoral fellow during the reporting period.

UR 7300 has not developed a policy of inviting foreign professors to consolidate its network of collaborators.

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 members of UR 7300 successfully applied for international and European calls for projects. During the present contract, a UR 7300 member coordinated one project and is currently coordinating two projects, all selected by ESA. The laboratory oversees work packages in five additional ESA projects.

UR 7300 is also partner of the 3BR Project 'Biomolecules and Biomaterials for the Regional Bioeconomy towards a "zero waste" valorisation' funded by the European Regional Development Fund and the Region Grand Est.

The members of UR 7300 are partners of national/international programmes (National Institute of Health, Sud Expert Plantes Développement Durable).

UR 7300 is involved in structures and projects funded by the Future Investments Programmes (PIA) with a leadership in one project 'Impact of a stress of the host on the diversity of intestinal microbiota and on resistance to antibiotics and a co-leadership in two other projects. UR 7300 is also partner of four projects funded under PIA.

The unit bids successfully in other national calls, all selected by CNES. It is also partner of one project in the framework of the CPER, one in the University's I-SITE, and numerous PHRC (e.g. SHARP, FAST-TB, RESPEDHEM, EVADE) with CHRU of Nancy.

Importantly, UR 7300 used its grants to invest 100.5 k€ to contribute to the funding of two PhD thesis and 27 k€ as internship grants for Master 2 students. New apparatus for a total of 326 k€ completed and renewed the equipment of the unit.

The GEPAM platform allowed giving a direct access to a variety of models, which is an original skill and a potential source of revenue via service provision.

Weaknesses and risks linked to the context

There is an absence of contracts from ANR thematic calls (young researchers (JCJC) for example) in the fields of immunology, microbiology and neuroscience to develop more in-depth studies on cellular and molecular mechanisms.

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

Strengths and possibilities linked to the context

Within the ACBS (Animal Facility of the Biology & Health Campus) animal facilities, the unit has created the original gravitational experimental platform, integrated in the ESA ground-based facilities portfolio. It is equipped with devices aimed at developing sophisticated animal (amphibians and rodents) but also cell culture models mimicking (gravitational and socio-environmental stress) both in ground level and space flight conditions.

The unit is trying to get a STAR-LUE label (Research Support Structure, Lorraine University of Excellence) for this platform, which would include the implementation of development, maintenance, renewal and quality strategies under the control of a quality research officer from the University of Lorraine.

The GEPAM platform is also open to the scientific community through a research announcement permanently opened by ESA. A first contract with IFREMER has been signed at the end of 2021. This agreement could open new long-term perspectives for research pertinent to space exploration.

The GEPAM platform is managed by a permanent staff with an engineer and a technician who are highly qualified.

UR 7300 engaged a large-scale renovation improving working conditions (new benches, fume cupboards, furniture etc.) with a global investment of 326 k€. This renovation has increased efficiency and facilitated scientific and technical exchanges.

Weaknesses and risks linked to the context

The certification of the GEPAM platform and its promotion through publications have created important expectations. Although the platform is fully operational since 2020 and visible on the ESA website, it is not yet involved in international projects resulting from external requests.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

With a mix of clinical and fundamental research publications on its core topic, the scientific production of the unit is excellent in terms of quantity and quality.

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

Strengths and possibilities linked to the context

The distinguishing scientific production of the unit concerns its original positioning around the effects of altered gravity but also chronic socio-environmental stress on immunity and gut microbiota. The unit enjoys recognition at the international level thanks to numerous collaborations and particularly via ESA grants.

Items 3 and 4 of the portfolio report important achievements of research on immune disturbances obtained in investigations of blood samples from (i) cosmonauts before, during and after a 6-month stay on the ISS, and (ii) volunteers who were subjected to a model mimicking microgravity. Articles related to these items are co-signed by international collaborators. Item 5 of the portfolio reports data showing that exposure to CUMS (Chronic Unpredictable Mild Stress, mimicking chronic psychosocial stressors encountered during spaceflight) induces significant change in murine intracaecal microbiota. This is an important achievement opening the way for further investigations in this field.

Among 47 peer-reviewed articles on fundamental research, 13 (28%), 1 review article and 10 book chapters (38% of the 26 book chapters produced) are directly related to this theme, dealing with analysis of cosmonauts' biological samples, of animals embarked on board BION-M1 biosatellite, or of animals submitted to stress mimicking space life conditions. These articles have been co-signed by international collaborators.

The unit sustains a regular production of original articles related to its core topic of stress-immunity-microbiota disturbances. Several of these were published in very good "generalist" journals (*Faseb J*, *Scientific Reports*). The unit published 142 articles in peer-reviewed journals including 47 on fundamental research and 95 on clinical research. 68% of the former are signed by members of UR 7300 in the first and/or last positions.

The unit promotes the emergence of original projects through a 10% levy on all contracts to support particularly initiatives led by young scientists (e.g. microgravity-induced physiological changes in *Fusarium* and role of dendritic cells in microgravity simulated conditions).

A clinical trial started in 2020 (European clinical trial Discovery, test of COVID treatments) is promising and well connected with the basic research theme of the unit.

Weaknesses and risks linked to the context

A clear match or connection between clinical investigations on one side and the principal basic research theme of the unit on the other side is lacking.

The microbiological topics investigated are somewhat dispersed and not clearly connected among them and with the principal theme of the unit.

Although the unit has significant potential to study the effect of stress mimicking space life conditions on behaviour and cognition, this has yet to be studied by its scientists.

The research projects of UR 7300 still lack from mechanistic studies.

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

MCU/PU and MCU-PH/PU-PH members of the unit devote a significant percentage (48% and 27%, respectively) of their time to research. The average scientific production is 2.85 per full-time lecturer-researcher per year.

All scientific staff of the Unit (MCU/PU and MCU-PH/PU-PH) have signed at least 1 article and 80% have at least signed 1 fundamental research article.

PhD students sign as first author and during the current contract, they have signed 20 basic research articles and 6 book chapters (43% of the articles and 23% of the book chapters produced by the unit). The second- or third-year PhD students currently present in the unit have all signed articles in the first author position.

Weaknesses and risks linked to the context

There is some disparity among the unit's scientist members concerning the number of publications and indicators of recognition, like the involvement in the organization of scientific manifestations, in learned societies.

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

Animal and human studies are conducted in accordance with all applicable national and European regulations (e.g. Lorraine Ethics Committee on Animal Experimentation, ethical standards of the Helsinki Declaration).

Experiments involving cosmonauts are carried out in accordance with the World Medical Association Helsinki Declaration and the protocols are evaluated by the Russian Ethical Board (Biomedicine Ethics Committee) and ESA Medical Board and the Russian Space Agency.

Animal studies are performed by qualified members including PhD students who hold the level 1 University diploma in animal experimentation. Five members of the unit are involved in evaluation of Animal Welfare.

The data traceability is ensured by digital recording and recording in laboratory books, and by archiving in public databases (e.g. the NCBI Sequence Read Archive) and their storage through the PETA service.

Decisions regarding scientific publications and unit's scientific policy are taken by formal (lab meeting) and informal exchanges between scientists involved in projects.

Weaknesses and risks linked to the context

None.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The overall contribution of research activities of the unit to society is very good.

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

Strengths and possibilities linked to the context

Several UR 7300 members were fully involved in the drafting of referential and international nomenclatures in learned societies, at ESA, in National Councils (CNU, Haute Autorité de la Santé, Agence Nationale de Recherche sur le SIDA).

Weaknesses and risks linked to the context

The unit develops several promising lines of research suggested to be relevant to societal stress and a sociocultural context (e.g. antifungal compounds, antioxidant polyphenols, and glaucoma model). However, the links with sociocultural context are a little bit overstated. It appears unclear if the spaceflight-associated research provides insights which serve public health or if, conversely, the biomedical insights and advances in research on ground-based populations may support and fertilize spaceflight-associated research.

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

Strengths and possibilities linked to the context

The GEPAM platform is now a ground-based facility of ESA and also referenced in "Plug in labs Lorraine". It creates new perspectives of academic collaborations as well as public-private cooperation.

A newly owned Luminex® 200™ system is unique in Nancy area and could open new resources via service provision.

UR 7300 developed a Soleau envelope in 2016 (n° 557352) concerning the development of a system to induce accelerated aging of B lymphopoiesis and bone structure, without pharmacological or surgical intervention and without stress for the animal.

In line with issues in space immunology, UR 7300 has developed interesting collaborations and PhD codirections with private companies in order to evaluate their different compounds of interest (e.g. C1N-102, polyphenols). UR 7300 obtained a contract (112 k€) with the company SEPTEOS SAS and a Cifre PhD grant on "Agroresources for space flight" (2019-2022). In a collaboration with the AVRIL group, another PhD programme was funded from I-SITE and a Cifre PhD grant was obtained (2022 -2025).

Another more recent collaboration with Axoltis Pharma aims to assess anti-inflammatory and neuroprotective properties. In this regard, the model of purified neuronal culture (retinal ganglion cells) developed by the laboratory is dedicated to in vitro tests. These tests could have a potential interest for the development of treatments for glaucoma, a condition that may be related to Spaceflight associated Neuro-Ocular Syndrome.

Weaknesses and risks linked to the context

Collaborative projects between private partners and UR 7300 are based on experiments in basic science and not on a declaration of invention owned by the laboratory. Even if this type of cooperation is source of funding for the training of PhD students, any results of interest for intellectual property protection remain the property of the private partners and cannot lead to patents or creation of start-ups.

The organization of GEPAM platform is not optimally adapted to its dual roles in academic collaborations and as service provision, since a single person will have to provide both services.

There is no further development resulting from the Soleau envelope deposit in 2016.

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 UR 7300 members have given conferences for the general public at the Museum-Aquarium of Nancy, at the Epinal planetarium and at the Maison de la Science Hubert Curien de l'Aube.

The unit's work is discussed in international media (e.g. The Federation of American Societies for Experimental Biology).

The members of UR 7300 have given national interviews about the biological impact of spaceflights ('Le Point' 2019 and 'Le Figaro' 2021, 'France Inter' 2021). Another field of research was presented in articles with local/national readership, concerning microbiota (Revue de la Recherche Médicale du CHRU de Nancy; Femina), and diabetes (Doctissimo website, Côté Santé).

The members of UR 7300 have given conferences in the context of continuing education (CANOPE conferences, Institut National Supérieur du Professorat et de l'Éducation INSPE Lorraine).

Weaknesses and risks linked to the context

None.

C - RECOMMENDATIONS TO THE UNIT

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

The unit should seek recognition of space immunology as a rare discipline by the University of Lorraine to apply for lecturer-researcher and PhD student recruitments.

Regarding the strong international visibility in the field of space life immunology, the skills in microbiology, the recent integration of neurobiologists and the creation of the GEPAM platform, in-depth mechanistic studies of the dialogue between the gut microbiota and the nervous and immune systems could be a suitable and exciting projection for the future and should be developed strongly.

Optimization of the GEPAM platform as service provision and a collaborative core facility will require the recruitment of a dedicated engineer.

The promotion of interactions and links between basic research and clinical projects should be amplified.

The unit should establish a data management plan.

The unit and its present and future directors should involve all unit's staff very actively in the transition of leadership and in the integration of the new neurobiologist members. A strong policy of transparent communication should be put in place to ensure positive forward-looking engagement of unit's staff for the upcoming years.

Recommendations regarding the Evaluation Area 2: Attractiveness

The unit's expertise is based on basic science including immunology, neurosciences and microbiology. The planning of an integrative research program integrating these fields would allow the emergence of major and original questions while using the platforms and expertise of the laboratory.

In this regard, a particular effort should be made to respond to calls for projects notably from the French National Research Agency (ANR) to get more substantial research funding. This could allow hosting post-doctoral researchers.

Another effort should be undertaken to attract invited foreign scientists and consolidate a research network, thanks to GEPAM facility as a ground-based facility of ESA.

Recommendations regarding Evaluation Area 3: Scientific Production

The scientific production of the unit could be improved by focusing the research activities on an integrative project including immunology, microbiology and neurobiology, allowing the evolution from descriptive approaches towards mechanistic ones.

The diversification of mild chronic stress models as well as access to astronaut faecal samples will offer opportunities to publish not only in disciplinary journals but also in higher ranking "generalist" ones, thus opening access to the unit's knowledge and know-how to wider scientific communities.

Funding acquisition and recruitment of PhD students by the new members of the unit will be important for maintaining a vigorous scientific production and innovation.

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

The committee encourages the unit to pursue active partnerships with private companies with the objective to obtain patentable results and perspectives of valorisation.

CONDUCT OF THE INTERVIEWS

Date

Start: 30 septembre 2022 à 08h30

End: 30 septembre 2022 à 18h30

Interview conducted: online

INTERVIEW SCHEDULE

8:30-9:00	Hcéres Committee meeting <i>Closed-door meeting</i>
9:00-9:05	Hcéres rules and procedures by M. Mercier-Bonin <i>Public session (all unit members)</i>
9:05-10:05	Scientific and administrative presentation of the Unit 20 min. Overall presentation of the Unit J.-P. Frippiat 10 min. Presentation of major results in immunology J.-P. Frippiat 10 min. Presentation of major results in microbiology C. Cailliez-Grimal 20 min. Discussion <i>Public session (all unit members)</i>
10:05-10:30	Committee debriefing and break <i>Closed-door meeting</i>
10:30-10:50	Meeting with ITAs (in French) <i>In the absence of any managing staff</i>
11:00-11:20	Meeting with researchers <i>In the absence of any managing staff</i>
11:30-11:50	Meeting with post-docs and students <i>In the absence of any managing staff</i>
11:50-13:00	Lunch break
13:00-13:40	Meeting with institution representatives: University of Lorraine, Pôle Biologie - Médecine - Santé <i>Closed-door meeting</i>
13:40-14:15	Committee debriefing <i>Closed-door meeting</i>
14:15-14:30	Break
14:30-15:00	Meeting with the Director of the Unit <i>Closed-door meeting</i>
15:00-15:15	Break
15:15-18:30	Redaction of the final report <i>Closed-door meeting</i>
18:30	End of the interview

GENERAL OBSERVATIONS OF THE SUPERVISORS

Nancy, May 26, 2023

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la Valorisation**

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Objet : General comments on the evaluation report - DER-PUR230023357 – SIMPA
(Stress, IMMunity, PAtHogens).

Dear Sir or Madam,

Thank you for the evaluation report made for the research unit SIMPA (Stress, IMMunity, PAtHogens), that you sent us on May 17, 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 SIMPA 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

Observations de portée générale:

Dear Sir/Madam,

We sincerely would like to thank the Chair and members of the committee for their evaluation and constructive comments about the research activities of the “Stress, IMMunity, PAtHogens” laboratory, as well as for the meaningful discussions held during the various sessions of the audition process.

We will take into consideration the recommendations of the committee and agree that close attention needs to be paid to promoting interdisciplinary and mechanistic studies in order to improve our scientific production and reach a wider audience. In this perspective, we have decided to focus our research strengths on two main axes (instead of three) i.e. the impact of chronic gravitational and socio-environmental stresses i. on the immune system and ii. on the microbiota and microorganisms.

Since many members of the unit are part of the University Hospital Center of Nancy, we will do our best to take advantage of this situation by promoting the implementation of collaborative clinical studies in connection with our research themes and results obtained in basic research.

We are aware that post-doctoral researchers are needed and intend to recruit post-doctoral fellows by applying for grants offered by the CNES, the ANR and the University of Lorraine (LUE program), and by seeking out candidates through our national and international collaborative network. We will continue our efforts to diversify funding sources by applying for financial supports from public research institutions and, through the CIFRE program or other financial supports, from private companies. We will also do our best to ensure that space immunology is recognized by the University of Lorraine as a rare discipline in order to apply for teacher-researchers and PhD students.

As indicated in the report, the implementation of a participative management to preserve the strong motivation of all members is crucial for the future of the unit. Since the audition of the laboratory on September 30, discussions and meetings were held where everyone spoke openly and freely about their concerns. This resulted in a formal discussion within the Laboratory Council which led, after a vote of the Council, to the non-integration of the new neurobiologists and the search for another director candidate. An experienced member of the unit, who has been part of the team since its creation and who is trained in team management, proposed his candidacy as director of the unit. This candidature has already been approved by the community.

We sincerely thank the committee for its insightful and constructive suggestions and hope that the University of Lorraine will recognize space life sciences as a rare discipline.

Yours faithfully,

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

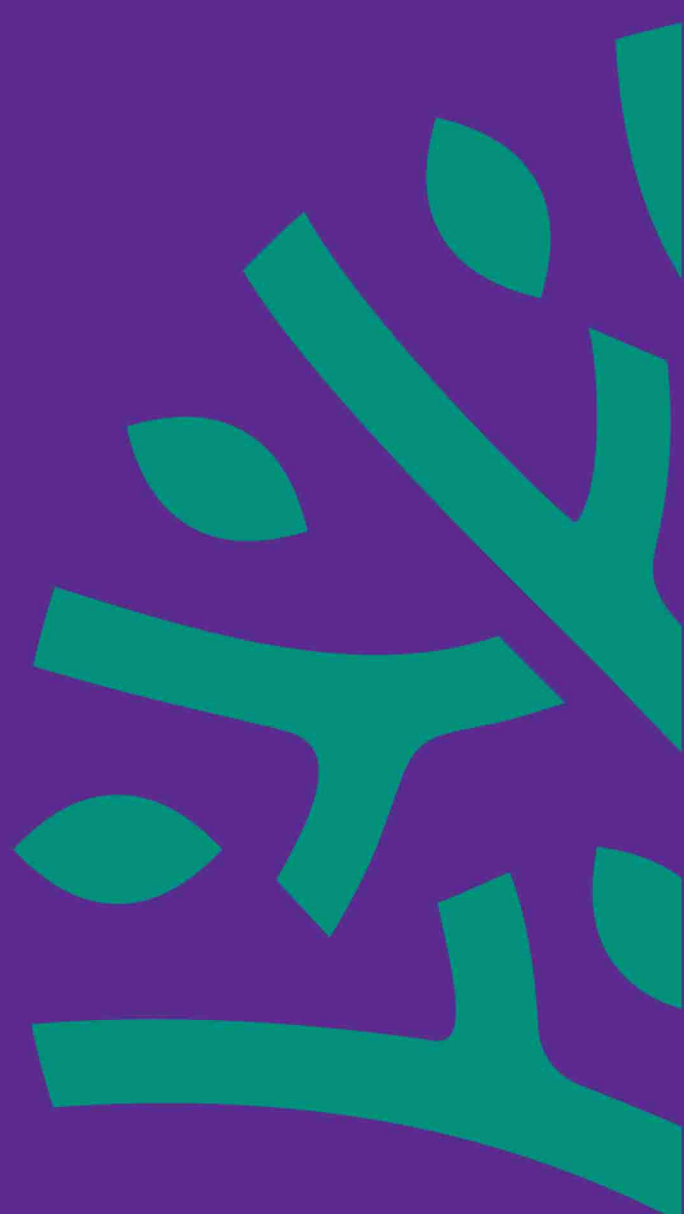
Evaluation of Universities and Schools

Evaluation of research units

Evaluation of the academic formations

Evaluation of the national research organisms

Evaluation and International accreditation



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