

Research evaluation

EVALUATION REPORT OF THE UNIT

B2A - Adaptation biologique et vieillissement

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Sorbonne Université

Centre national de la recherche scientifique – CNRS

Institut national de la santé et de la recherche médicale – Inserm

EVALUATION CAMPAIGN 2023-2024GROUP D

Rapport publié le 19/01/2024



In the name of the expert committee $^{\scriptscriptstyle 1}$:

David Bernard, Chairman of the committee

For the Hcéres² :

Stéphane Le Bouler, acting 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 estab_tab1lished by the expert committee and signed by their chairperson." (Article 8, paragraph 5).



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

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

MEMBERS OF THE EXPERT COMMITTEE

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CHARACTERISATION OF THE UNIT

- Name: Adaptation biologique et vieillissement
- Acronym: B2A
- Label and number: UMR SU CNRS 8256, Inserm as ERL U1164
- Composition of the executive team: Mr Bertrand Friguet and Ms Rachel Sherrard

SCIENTIFIC PANELS OF THE UNIT

SVE6: Human Physiology and Physiopathology, Ageing

SVE3: Living Molecules, Integrative Biology (From Genes and Genomes to Systems), Cell and Development

Biology for Animal Science

SVE5: Neurosciences and Nervous System Disorders

THEMES OF THE UNIT

The unit develops a multidisciplinary research program, fundamental and curiosity-driven, in order to better understand the cellular adaptation to stressors throughout life and the factors controlling healthy ageing and vulnerability to age-related diseases. Whenever possible, the unit also develops translational projects to evaluate potential therapeutic and preventive strategies to impact cellular, tissue, and whole organism ageing. The eight teams composing the unit each address specific questions with complementary expertise and models, often investigating similar biological processes. Teams are involved in one or several of the following four main themes:

- (i) fundamental processes controlling cell physiology (team 1: Cryptochromes and stress responses, team 2: Oxidative stress and cellular senescence, team 3: RNA translation, team 4: Gene regulation and systemic biology, and team 8: Chromatin, epigenetic and RNA biology);
- (ii) mechanisms controlling neuronal dysfunctions (team 4: Cell death and neurodegenerative diseases, team 5: Genes and pathways in synapse stabilization, and team 6: cAMP/PKA pathway);
- (iii) mechanisms involved in cardiovascular diseases (team 2: Vascular cellular senescence, cardiac function, team 6: Mechanisms controlling cerebrovascular integrity, and team 7: SRF and mechanisms leading to cardiac diseases);
- (iv) regenerative biology applied to cardiac muscle repair (team 7: Stem cell-based therapy) and neural circuit dysfunction (team 5: magnetic fields for neuro-degeneration and Alzheimer disease).

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The UMR CNRS 8256 "Biological Adaptation and Ageing" (B2A-IBPS) was created in 2014 and renewed in 2019. The unit is located in the Cassan building at the Pierre et Marie Curie Campus of Sorbonne University, and is part of five constituent research units of the Institute of Biology Paris-Seine (IBPS), a research federation (FR 3631) providing access to important platforms (including an imaging facility). Six teams originated from the previous unit, one (team 7) resulted from the fusion of two teams from the previous unit, and one (team 8) joined the unit in 2020 from the Pasteur Institute. Two teams (2 and 7) are also affiliated with Inserm as ERL U1164.

RESEARCH ENVIRONMENT OF THE UNIT

B2A-IBPS is one of the few CNRS units to have a theme centered on ageing. It is part of the IBPS research federation of Sorbonne University that aims to increase quality and visibility of biological research performed at the Jussieu campus by fostering collaboration between scientists of different fields (ageing, development, neurosciences, computation biology and physics). IBPS supports research by providing access to important platforms and by sponsoring shared PhD students between B2A and other IBPS units, and units of the Sorbonne University faculty of Science and Engineering. Sorbonne University Idex funding (Emergence program, ISIM, and i-Bio initiatives) also support interdisciplinary PhD students with shared programs and supervision between Sorbonne University units. Several B2A teams are also partners of Labex programs (Biopsy and Revive).



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

Catégories de personnel	Effectifs
Professeurs et assimilés	11
Maîtres de conférences et assimilés	14
Directeurs de recherche et assimilés	6
Chargés de recherche et assimilés	8
Personnels d'appui à la recherche	21
Sous-total personnels permanents en activité	60
Enseignants-chercheurs et chercheurs non permanents et assimilés	6
Personnels d'appui non permanents	8
Post-doctorants	5
Doctorants	23
Sous-total personnels non permanents en activité	42
Total personnels	102

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

Nom de l'employeur	EC	С	PAR
SORBONNE UNIVERSITÉ	25	0	14
CNRS	0	9	5
INSERM	0	5	1
AUTRES	0	0	1
Total personnels	25	14	21

GLOBAL ASSESSMENT

The B2A unit "Adaptation biologique et vieillissement" is composed of eight research teams (102 members total) housed in the Cassan building on the Pierre et Marie Curie Campus. It is part of the Institute of Biology Paris-Seine (IBPS) that provides access to numerous platforms. The unit develops multidisciplinary research programs on ageing and age-related diseases to better understand fundamental processes regulating aging (at the cellular, tissue and organism level), and when pertinent to develop preventive or therapeutic strategies for age-related diseases and to improve healthy aging.

Overall, the level of publications of the unit in leading position ranges from very good (e.g. *Plos Biol, Cell Death Dis, eLife*) to excellent (*Science Advances, Circulation*). The unit published a total of 257 articles, including 200 original research articles. 45% of these involved unit member as first, last and/or corresponding authors. Major advances during the mandate include original work on the impact of blue light or magnetic field exposure on cellular processes such as ROS signaling and neuron connectivity.

Overall, the attractiveness of the unit is very good to excellent. Training through research is very good: 54 PhD students trained for 28 HDRs, and 36 theses defended during the period. Nevertheless, the difficulty in attracting young leaders, the continuous decrease in unit members, and the fact that many team leaders are reaching retirement age, are important issues. Research activity of the unit is supported by an excellent level of funding. Of the 15 million euros of total credits obtained over the last period, about 13 million euros (85% of the total) were secured by individual teams. An additional 2 million were recurrent funding from institutions (CNRS, Sorbonne University and Inserm). Most external funding (75%) was obtained through national calls, with 2 PIA, 7 ANR, 1 INCA and 1 FRM as coordinator, and an additional 3 PIA and 7 ANR as partner. They are partners in four European projects. International funding (10% of total) included grants from the Leducq foundation (575 k€ as leader) and the CHDI foundation (1.4 M€ as leader). The remaining funding was from local and regional calls (5%).

Specific technical expertises of the unit includes the capacity to identify the complete "Oxiproteome" of a given tissue or cellular extract, biosensor imaging in vitro and in vivo, genomic system biology, disease modeling using



human stem cells and 3D cell culture, and mouse-adapted innovative tools for repetitive transcranial magnetic stimulation.

The unit is excellent at communicating their research at different national and international meetings (125 invitations, including Gordon Conferences and Society for Neuroscience meeting). It is also excellent at organizing national and international meetings (Gordon Conferences, Society for Neuroscience) as well as one summer school (IBPS Summer School on Optical Biosensors). The unit is also involved in national and international collaborative projects and networks on aging and age-related diseases (for instance AGEMED 1 & 2, Labex, AFSOR, NSF, Leducq and CHDI Foundations, EU COST) demonstrating strong involvement in networking in their research field.

The contribution of the unit to society is excellent: 14 contracts obtained with private companies (for instance with Partnership with ND-Bioscience (Lausanne), Beckmanm, LVMH), two Cifre fellowships, six filled/deposited patents and 1 start-up created. The unit also intervened in events for a broad audience (for instance Fête de la Science, journées Portes Ouvertes and the Café des Sciences).

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The main recommendations were taken into account:

"The unit should increase the publications" in higher profile journals.

The unit's publication record has improved.

"The unit should increase the number of intra-unit seminars and journal clubs."

Regular seminar series have been conducted. The B2A unit also participated in organizing the seminar series of the research federation IBPS. B2A members organized the 2022 *i-Bio* mini-symposium (half day), and B2A members co-organized the very first IBPS Summer School on Optical Biosensors.

"The Laboratory Council should become more functional and convene more regularly."

Efforts have been made to convene the council three times per year. Social events at the unit level were also organized.

"The unit should provide organized/formalized assistance to foreign researchers (PhD students, Postdocs)"

The administrative support staff of B2A worked in close collaboration with the FSI International Mobility Office. Assistance to foreign researchers (PhD students, Post-docs) has been greatly improved.

"The unit should optimize organizational aspects collectively for more efficient administrative support."

The administrative support staff of the B2A unit has been strengthened by the arrival in September 2021 of a new administrator.

"The unit should create a list of intra-unit duties for each permanent staff. It helps to participate in unit's organization by sharing responsibilities."

Due to the location of the B2A teams on 5 different floors, a floor-by-floor organization of the duties in close connection with the neighboring units, rather than an intra-unit organization, was preferred.

"The unit should improve bilateral interactions among teams with closely related topics and overall. interactions among all research teams of the unit."

The recommendations on scientific strategy and projects were taken into account. Bilateral interactions between teams have been quite active and have led to the publication of several collaborative papers within B2A.

"The unit should increase interaction with clinicians and clinical trials."



Two teams hosted a PUPH, linking B2A-IBPS to clinical structures, while several B2A teams are involved in collaborative projects with clinicians on topics such as Alzheimer and Huntington diseases, heart failure and reaeneration.

"The unit should decrease the diversity of projects and enhance the focus on the core topics of ageing."

Each team has tried and, depending on funding opportunities, usually succeeded in decreasing the diversity of their projects to continue focusing on topics related to ageing.

B - EVALUATION AREAS

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

Assessment on the scientific objectives of the unit

The scientific aims of B2A are very good: the focus on aging at the molecular, cellular, tissue and whole organism level is a rare example in France. The theme of each team is well-defined, and in most cases, clearly in line with the general topic of the unit. B2A has a clear vision of the scientific field at the national and international level. Nevertheless, the unit suffers from the lack of a clear strategy to attract new teams on complementary topics, limited numbers of clinicians to facilitate transfer, and difficulties in maintaining permanent staff and the associated technical know-how.

Assessment on the unit's resources

The unit attracts an excellent level of funding from different sources and benefits from very good visibility in their research field. Nevertheless, there is a strong inter-team heterogeneity in funding levels and visibility. The unit suffers from a continuous decrease in the number of permanent staff members since the previous contract. Additionally, several PIs are close to retirement.

Assessment on the functioning of the unit

The unit's organization is very good, but challenged by operational difficulties: dispersion of teams over five floors hampers intra-team collaborations and communication among staff. The urgent need to renovate the occupied buildings is difficult to reconcile with the maintenance of high-level scientific activity. This difficulty is exacerbated by the lack of technical support staff for facilities, administration, and teams.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

Lifespan expectancy has increased during the last decades, whereas improvement of healthy lifespan during the same period was limited. The B2A unit tries to tackle this societal challenge by developing projects to better understand fundamental processes regulating aging and age-related diseases with the long term aim to improve healthy aging. Most of the teams have developed research axes clearly in line with this general topic of the unit, from general fundamental questions (for instance, response to stress, cellular senescence) to more applied scientific questions on neuronal dysregulation and cardiac diseases. The general organization and administration of the unit and of IBPS provides support and access to platforms.

Weaknesses and risks linked to the context

The projects of a few teams do not appear to be directly in line with the overall scientific objectives of the unit on aging and age-related diseases.



Transfer and clinical activities are limited in spite of the ambition of the unit to test new strategies to improve aging and age-related diseases.

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

Strengths and possibilities linked to the context

Activities of the B2A unit are largely dedicated to research (50% research, 20% valorization, 10% training, 5% dissemination...), which is in line with the expectation of an UMR coupling university and CNRS/Inserm research bodies. Unit activities are carried out by 60 permanent staff members (14 full time CNRS or Inserm researchers, 25 Professors and Assistant Professors, and 21 technical staff) and by 28 PhD students and postdocs, and 8 research officers/technicians.

Between 10-15% of total resources (282-306 k \in per year) were provided by the CNRS (140-160 k \in per year), Sorbonne University (82-115 k \in per year) and Inserm (40-46 k \in per year). Additional resources (1600–2575 k \in /year) were obtained from local supports (0-246 k \in /year from regional funds, Labex...), national competitive grants (1200-2100 k \in /year from ANR, FRM...), international grants (0-550 k \in /year from the Leducq Foundation, CHDI...), and valorization, transfer or collaboration with private companies (90-300 k \in /year, SATT, LVMH...).

Weaknesses and risks linked to the context

Although all teams are headed by established scientists, there is a strong heterogeneity in terms of technical support staff and available resources.

An active unit program dedicated to attracting new teams with complementary research themes or to promote inter-team collaborations is absent. Indeed, although resources obtained by the different teams represent 85-90% of the available resources in the unit, none of these were used to implement a shared, pro-active scientific policy to strengthen inter-team collaboration.

Clinicians are largely under-represented and none of them lead teams, impeding potential transfer of unit discoveries to clinical applications.

Several teams are headed by scientists reaching retirement age.

There was a decrease in both permanent and non-permanent staff numbers since the previous contract.

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

Strengths and possibilities linked to the context

Within the unit, gender parity for the permanent staff is globally respected with a women-to-men ratio slightly favoring women (52/38). Among researchers the ratio is very well balanced (26 women/30 men). Health and safety obligations are fulfilled by three prevention assistants (APs), with one person fulfilling the role of Radiation Protection Officer. The competent person in radioprotection is in charge of ensuring that safety instructions concerning the possession and use of radioactive materials are respected.

Health and Safety issues are well managed with the single risk assessment document updated annually, the periodic inspection of equipment and the appropriate disposal of hazardous waste. Authorizations for the use of OGMs and radioactivity were obtained.

Intellectual property is secured by nominative laboratory notebooks of which the laboratory retains the property. The electronic files are secured by server back-ups.

The unit has a clear staff hosting policy. Arriving personnel is introduced to the Unit's Directors and Administrators, and the unit works in close collaboration with the FSI International Mobility Office to integrate newcomers. A "Doc & Post-doc" Association of IBPS provides social support for new arrivals.

Weaknesses and risks linked to the context



Within the research support staff, the women-to-men ratio (26/8) is noticeably skewed towards women, while for the leading PI positions women are underrepresented (3/7).

There is no easy access to computer security services, for instance encrypting work laptops.

There is no RPSS (mental health committee).

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The attractiveness of the unit is excellent in securing funding and invitation to congress (e.g. Gordon conference). The unit obtained numerous national (75% of the unit funds comes from PIA, ANR, INCA, FRM) and international (Leducq Foundation) grants through competitive calls for projects. They are partners of 4 European projects.

The unit is also actively involved in several international collaborations and networks (e.g. EU COST action. However, the unit experienced difficulties in maintaining personnel due to problems tied to the local environment (for instance outdated infrastructure). Since 2017, B2A-IBPS only attracted six MCU and seven CR/DR researchers. More than 15 PhD scholarship and post-doctoral fellowships were obtained from Labex, lle-de-France region, charitable trusts and industry.

- 1/ The unit has an attractive scientific reputation and is part of the European research area.
- 2/ The unit is attractive because for the quality of its staff support policy.
- 3/ The unit is attractive through its success in competitive calls for projects.
- 4/ The unit is attractive for the quality of its major equipment and technical skills.

Strengths and possibilities linked to the context for the four references above

Members of B2A attended international and national meetings and congress (125 invitations as speakers, session chairs, or selected oral communications) and organized or contributed to the organization of international meetings (Gordon Conferences, Society for Neuroscience meeting). B2A members also organized a minisymposium (Senescence: from fundamental mechanisms to drug discovery) and a Summer School (IBPS Summer School on Optical Biosensors).

Four teams (1, 2, 4, 5) are partners in European and International projects or networks (AFSOR, NSF, Leducq and CHDI Foundations, EU COST). Altogether, European and international grants accounted for 165-550 k€/year.

Several B2A-IBPS teams belong to national research excellence networks including AGEMED 1 & 2, Labex "BioPsy" or "Revive". Other teams have received support from regional initiatives such as DIM Longévité of the Region lle de France (Gerond'if). The unit also secured regional funds for technology transfer (eg SATT Lutech, CNRS, Inserm).

Some unit members acted as experts for international and national grant agencies (NIH, ERC, H2020, ANR, NSF) and for foundations (AFM, FRM). Team leaders or senior investigators served on local or national evaluation committees for the Hcéres, Inserm, CNRS, and the National Council of Universities, and local committees of Sorbonne University. Most of the permanent B2A staff participate in recruitment committees (assistant PR, PR, tech). Others served in scientific societies (GRRC, SFGG, etc), scientific committees (GDR 2588) and trustees (e.g. Gerond'IF).

Two team leaders participated in the creation of an Erasmus Mundus Joint Masters (EMJM) program in Aging. Many of the research members of B2A are Sorbonne University faculty actively involved in research training and development of highly visible innovative teaching programs. B2A staff members head Masters Programs in



"Molecular and Cellular Biology" and "Integrative Biology and physiology", including the International Master in Brain and Mind Sciences (with UCL). More than 15 PhD scholarship and post-doctoral fellowships were obtained from Labex, lle-de-France region, charitable trusts and industry.

The involvement of several PIs in local, national and international activities allows them to have a global vision of national and international competition.

The unit created an in-house technical service thanks to a grant obtained in 2021, allowing recruitment of one technical personnel. The service focuses on the development of human induced pluripotent stem cells (iPSC) for modeling diseases associated with aging and screening therapeutic molecules. The unit has access to IBPS technical facilities including the IBPS Imaging Facility, which provides flow cytometry, photonic and electron microscopy, the ARTbio bioinformatics facility, the proteomics facility.

Several technical platforms ("plateau techniques") were established including the "PhenoHeart" and "2D and 3D cell culture platforms" (team 7), the SeaHorse platform (team 2), and machine learning platforms (team 4).

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

The unit has shown limited recruitment capacity (only six MCU and seven CR/DR researchers recruited since 2017). During the same period, six CR/DR, two MCF and one PUPH left the unit. Three technicians, three AI, two IE and one AJT also left the unit, and only two technicians, four AJT, two AI, two IE and one IR replaced them. Recruitment of new young researchers is very weak, with only one CR (CNRS) recruited in 2018 who then left the unit in 2021. 33 PhD students defended their thesis for 34 HDRs.

Expert appraisal activities and responsibilities on national and international academic and non-academic boards are carried out mainly by team leaders or a limited number of senior researchers. The same applies to responsibilities for funding applications and collaborative networks. The apparent hegemony of certain senior researchers of high national and international repute, could be a concern for the future contract considering that several PIs may retire during or at the end of next contract.

Given the size of the unit, the number of European projects or grants is modest, especially in the role of coordinator. Success in calls for tender is very heterogeneous from one team to another.

The current level of technical staff numbers appears to be insufficient. The chronic loss of technical staff, through mobility or retirement, fragilizes not only the facilities, but also the different teams that risk losing expertise.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The scientific production of the unit is very good to excellent: 257 papers in total, 112 as first, last or corresponding author published in journals such as *EMBO J, Science Advances, NAR, Circulation*. The number and quality of publications is quite heterogenous within the unit, as in the number of shared publications between unit teams.

- 1/ The scientific production of the unit meets quality criteria.
- 2/ The unit's scientific production is proportionate to its research potential and properly shared out between its personnel.
- 3/ The scientific production of the unit complies with the principles of research integrity, ethics and open science. It complies with the directives applicable in this field.

Strengths and possibilities linked to the context for the three references above

Based on available data, the scientific production of the unit reflects well the scientific and technical expertise of its teams. The unit shows an excellent level of scientific publication in terms of quantity: 200 original research



papers, and 57 reviews or book chapter; members of the unit were first, corresponding or last author in approximately 45% of original articles, the rest were collaborative papers.

Publications were in very good to excellent journals, either generalist (Elife, Aging Cell, PloS Biol, PloS Genet, Cell Death Dis, Cell Death Differ, EMBO J, Science Advances, NAR) or more specialized ones (J Invest Derm, J Med Chem, Acta Biomater, Circulation).

PhD student and postdoctoral fellows signed as first authors in about 30% of the original articles published by the unit, which is good.

The scientific production of the unit respects the principles of scientific integrity, ethics, and open science. It complies with the applicable guidelines in the field. Electronic files are systematically backed up on distant servers for data recording and preservation and patents are lodged for appropriate results. All experiments involving animal and human tissues follow ethics rules according to French and European law. Applications for animal experiments are submitted to ethics committees and conducted under the responsibility of a scientist having the authorization from "Direction Départementale des Services Vétérinaires de Paris". It is mandatory that PhD students and post-doctoral fellows undertake official animal experimentation training.

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

The level of publication is not uniform among the teams (even when normalized to the number of team members).

The number of publications in highly reputed journals could still be improved to strengthen visibility of the unit.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The unit demonstrates a consistently very good to excellent level of engagement with both industrial partners (14 contracts, two Cifre) and the general public (patient associations, public outreach). Six patents were filed and one start-up was created (BioGemix). However, these activities are quite heterogenous among the teams.

- 1/ The unit stands out for the quality and the amount of its interactions with the non-academic world.
- 2/ The unit develops products for the cultural, economic and social world.
- 3/ The unit shares its knowledge with the general public and takes part in debates in society.

Strengths and possibilities linked to the context for the three references above

B2A actively established interactions with non-academic partners, hosting several researchers from small and medium-sized enterprises (SMEs) or start-ups, and offering services. They have established bilateral collaborations or partnerships with several SMEs but also larger companies. This is also reflected in the significant industrial funding they have obtained, including several non-university PhD stipends (among them two Cifre), 14 industrial contracts (for example, Partnership with ND-Bioscience (Lausanne) (80 k \in) for the co-development of innovative neuroprotective agents in the context of synucleopathies, Subcontracting to Beckmanm (20 k \in), LVMH Dior Cifre accompanying contract on glyoxal induced keratinocyte senescence (120 k \in), Creation and supervision of professional courses for Sanofi "Therapeutical proteins: challenges and innovations" (30 k \in).

Six patents were deposited since 2017 (three by team 2, one by team 4 and two by team 7). Team 4 established a start-up company (BioGemix).



A team member has also supervised professional courses for Sanofi pharmaceutical company while members from two teams (team 4 and team 6) have established close interactions with patient associations related to age-associated neurodegenerative diseases.

The unit is involved in a multitude of activities ranging from participation in public outreach programs ('fête de la Science', 'journées Portes Ouvertes' and the 'Café des Science's), delivery of lectures to the general public and undergraduate students, active participation in "Sorbonne Summer School", interviews in newspapers and websites and press coverages following their scientific publications. This strong presence is linked to the clear public interest of the unit's thematic (ageing and longevity). PhD students of the unit are highly involved in dissemination activities through their participation in the "My Life as a Researcher" program, aimed at high school students.

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

Not all teams are involved in general public interactions. Apart from the interaction with neurodegenerative diseases patient associations, interactions with patient associations for other age-related diseases are not present. Only two teams (team 1 and team 2) present activities related to interactions with schools.

ANALYSIS OF THE UNIT'S TRAJECTORY

The unit is facing a number of difficulties: several leaders will retire soon, the balance between arrivals and departures is negative, and the unit has had difficulties to sustain technical know-how because of lack of permanent technical staff. In this context, the unit, and two of the eight teams, will close at the end of this contract. Most of the remaining teams will join a new bigger unit "Development, Adaptation, and Ageing (Dev2A)" at the IPBS, while two teams will join other units within IBPS.



RECOMMENDATIONS TO THE UNIT

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

The unit will close. N/A.

Recommendations regarding the Evaluation Area 2: Attractiveness

The unit will close. N/A.

Recommendations regarding Evaluation Area 3: Scientific Production

The unit will close. N/A.

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

The unit will close. N/A.



TEAM-BY-TEAM OR THEME ASSESSMENT

Team 1: Photobiology

Name of the supervisor: Ms Margaret Ahmad

THEMES OF THE TEAM

The team studies the structure and function of the cryptochrome blue light receptors in plants and other organisms, and their involvement in the response to magnetic and radiofrequency fields. The team is also interested in assessing the infrared and magnetoreception mechanisms involving cryptochromes and developing novel biotechnological applications.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has followed the recommendations of the precedent Hcéres evaluation.

"The team is urged to maintain the productive stream and further pursue ground-breaking research and high impact publications."

The team has increased its production (20 papers for the evaluation period). The research portfolio of the team has been expanded to include new research lines which could have a significant impact on improving public health.

"The team could be strengthened with additional members in selected areas of research". The team has increased in numbers (from 9 to 15 during the evaluation period)

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	4
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	2
Post-doctorants	0
Doctorants	1
Sous-total personnels non permanents en activité	3
Total personnels	7

EVALUATION

Overall assessment of the team

The team carries out original and pioneering interdisciplinary research on the role of cryptochrome blue light receptors in the response to magnetic and radiofrequency. The scientific production is very good to excellent: 20 papers published in the last period, including *J. Cell Sci, PLOS Genet* as leading author). The attractiveness of the team is very good: nine invitations to international congresses (two Gordon), four international collaborations (for instance AFOSR, NSF), collaboration with private company (LMK, trial 360°), co-editors of two special topic article series in Frontiers in Plant Sciences, and recruitment of four foreign scientists. The training through research activities is very good (six PhDs trained, undergraduate teaching, and organization of summer courses). The societal valorization and outreach of the team are very good (interactions with medical professions and companies interested in light therapies).



Strengths and possibilities linked to the context

The team is composed of 1 DR CNRS, 2 MCU SU, 1 TECH SU, 1 AI CDD and 2 PhD students. It pioneered the investigation of the role of the cryptochrome blue light receptors in the response of plants and mammals to magnetic and radiofrequency fields. The scientific production of the team is very good to excellent with 20 papers (90% of them as first or last author positions) in both specialised and generalist journals (J. Cell Sci, PLoS Genet, PLoS One, etc). Team members have been invited to 9 international conferences, including 2 Gordon conferences.

During the evaluation period the team attracted more than 0.5 million Euros in competitive national (CTM, SCAC) and international calls (such as Novo Nordisk, PHC, NSF, etc), which is a very good to excellent level of funding for a small team. They also received regular funding from private companies, such as LMK (135 $k \in$) and the company "trial 360°" for a pre-clinical trial on the use of infrared light for the treatment of hyperinflammation of COVID-19 (200 kUSD).

A total of six PhD students were trained for a total of two HDR, and four completed their thesis with publications as first author.

Members of the team have co-edited a special topic article series.

Some outreach activities are reported such as interactions with medical professions and companies interested in light therapies.

Weaknesses and risks linked to the context

The visibility of the research field is still limited. They have not yet established an independent brand in the field of aging. Limited/no postdoc staff and economic valorisation.

Analysis of the team's trajectory

Since its creation in 2014 the team has followed a rising and dynamically evolving trajectory: from their pioneering works on the cryptochrome to their findings of the effects of electromagnetic fields on cryptochromes that in turn induce a transient change in the formation of Reactive Oxygen Species (ROS).

The new project will focus on the effects of electromagnetic fields on ROS signaling pathways, which might have important implications linked to the exposition of electromagnetic waves (mobile phones, etc). The unit is closing and the team will join a new unit "Development, Adaptation and Ageing" Dev2A.

RECOMMENDATIONS TO THE TEAM

The team could further strengthen interdisciplinary collaborations with other disciplines linked to the use of medical radiations.

The team should put in place a strategy to attract and recruit postdocs eligible for CRCN recruitment as a long-term strategy of the team.



Team 2: Integrated cellular ageing and inflammation

Name of the supervisor: Bertrand Friquet (Future team leader: Chahrazade El Amri)

THEMES OF THE TEAM

Team 2 aims to: 1) decipher the processes that govern ageing at multiple levels (molecular, cellular, tissue and integrative) and, 2) identify preventive and regenerative approaches that will counteract deterioration due to ageing. Among the hallmarks of ageing, team 2 has addressed cellular senescence, impaired regenerative capacity, mitochondrial dysfunction, loss of proteostasis (proteasome, LON, kalikreins and caspase 2) and inflammageing. The team has investigated the role of the above players in the ageing process and identified modulators of these players.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

It was recommended that the team should promote association with European and international partners to increase the quality of published articles, increase its capacity to supervise PhD students, and further invest itself in various teaching programs to attract more students. The team tried to take into consideration these recommendations: recruitment of 13 PhD students (seven finished in 2022, five will finish in 2023, one just started) and 5 post-docs (two finished in 2022, one in 2023 and one just started).

It was also recommended that the team should recruit a full-time researcher to reinforce its workforce, to attract a new engineer and more PhD students and to equilibrate the identified gender issue (in the previous period, the number of women largely exceeded that of men). Two recruitments took place in 2022 and 2023, and one more is planned in 2025. Moreover, the next team leader is already secured. The gender ratio is still not balanced (more women than men). Concerning the infrastructural problems mentioned in the previous report, a partial renovation of specific spaces has occurred while University funds from PEPR have been committed for general renovation before the end of 2025.

Establishment of collaboration with clinicians was suggested. The team published three clinical articles and works with clinical specimens, addressing this issue. Closer collaboration with previous team 8 (Team 7 in this period) was established (two papers already).

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	4
Maîtres de conférences et assimilés	3
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	12
Enseignants-chercheurs et chercheurs non permanents et assimilés	4
Personnels d'appui non permanents	0
Post-doctorants	1
Doctorants	8
Sous-total personnels non permanents en activité	13
Total personnels	25



EVALUATION

Overall assessment of the team

The overall scientific output of the team is excellent with 34 original research articles (2/3 in leading positions) in excellent specialty (e.g. *Circulation, Cardiovasc. Res, Free Rad Biol Med*) and more generalist (eLife) journals. The team's overall attractiveness is excellent with funding from international agencies such as the Fondation Leducq (575 $k\in$) and industrial contracts. The team trained 13 PhD students and 5 post-docs. The valorisation of the team is excellent with 3 patents (2 of which with pre-maturation and maturation programs), 2 industrial contracts (1 Cifre), and extensive communications to the public.

Strengths and possibilities linked to the context

Team 2 is composed of 4 PU, 3 MCU, 1 CR, 1 AI, 1 engineer and 6 PhD students, and is proactive in maintaining its composition in view of the upcoming retirement of advanced scientists.

The team published 34 research articles (22 in leading position and 12 collaborative ones), 7 reviews (5 in leading position) and 5 book chapters (4 in leading position). Publications are in excellent quality scientific journals (Circulation, Cardiovasc. Res, Free Rad Biol Med, eLife).

The team is effective in attracting funding from international (Partner of Foundation Leducq grant; 575 k€, 2017-2023), national (e.g. 3 ANR contracts with 1 as coordinator 157 k€) and charities (5 as PIs; for instance, Fédération française de cardiologie, 100 k€, 2023-2025; Ligue Nationale contre le cancer, 25 k€, 2022-2023) for a total of 1 840 k€ over the evaluation period.

The team is strongly implicated in training, with 13 PhD students (seven finished in 2022, five will finish in 2023, one just started) that all have publications (either in preparation or already published) as first authors. The team leader and researchers are strongly implicated in research networks and doctoral programs. The team hosted five post-docs (three foreigners; two finished in 2022, one in 2023). All postdocs (with the exception of the one who just started) have published (one manuscript in preparation and two published).

Team members are invited to various meetings (28 invited or selected oral communications), including international ones (FEBS and EMBO Conferences). PhD students from the team have participated with presentations at international schools or meetings (e.g. FEBS Advanced Course "Redox Alterations and Cellular Responses: From Signalling to Interventions" and the 7th International Symposium on kallikreins and kallikrein-related peptidases). Team members were also implicated in the organization of 2 national and 2 international meetings/symposia.

The team PI is editor-in-chief of Biochimie. Several members serve on editorial boards of scientific journals without however mentioning specific numbers. Team members obtained 4 prizes: Henner Greaff Young Investigator award and 3 awards/prizes to PhD students of the team: SOS Oxygen and FEBS Open Bio awards and a prize for best talk in a national meeting (GRRC: Printemps de la cardiology).

Team 2 founded one start-up company (OxiProteomics, initiated in 2015), had strong interactions with industry (e.g. ND-Bioscience with a contract of 80 k€ and LVMH DIOR through a Cifre contract of 120 k€) and filed three patents.

Weaknesses and risks linked to the context

No EU funding is reported. No mention of links to patient associations.

Analysis of the team's trajectory

For the next contract, team 2 will join a new research unit, namely Dev2A unit at IBPS. The current team leader will retire before the end of the next period (2025-2029) and a researcher has been appointed to lead the team.

RECOMMENDATIONS TO THE TEAM

The team should try to attract more PhD students and post-docs in the next evaluation period since most of the previous ones have completed their PhD (either in 2022 or in 2023). This is important for know-how transfer. The team may also consider increasing the number of HDRs as previously suggested.

The team should put more efforts on attracting EU-funding. They should also try to increase the common projects/papers with the other teams in the unit (as they have already done with Teams 6 and 7). They should also strive to include clinical specimen more systematically in their work. Finally, further efforts should be made to interact with schools, patient associations and the general public. Recruited MD/PhD students and clinical researchers (PU/MCU-PH) could also help raise awareness to patient associations.



Team 3: Eukaryotic Translation, ET

Name of the supervisor: Mr Olivier Jean-Jean

THEMES OF THE TEAM

Translational regulation is a key mechanism to rapidly change gene expression in response to stimuli. The team focuses on (i) the role of upstream ORFs (uORFs) in gene expression, (ii) the role of translation termination in mRNA degradation and (iii) the modification of tRNAs by flavoenzymes.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations of the previous report were to intensify fundraising and to increase the number of publications relative to the number of permanent staffs (currently six people). Lack of visibility and interactions with the non-academic world were also mentioned.

Efforts in fundraising were made, and the future potential PI of the team obtained funds as coordinator of a bilateral ANR-DFG grant (French-German collaboration), 2021-2025, 190 k \in , and of a regional grant from the IBPS, 2020-2021, 20 k \in .

During the current evaluated period, 4 original research articles were published as main authors (*Biochimie*, 2021; *RNA Biol* 2020; *NAR*, 2018; *Oncotarget*, 2018) and 7 collaborative publications. The number of publications has thus increased.

Non-academic interactions were improved with a technology support contract with the EUKARYS company, leading to a publication in collaboration (*NAR*, 2019).

The future potential co-PI of the team was editor for a topical collection of the Non-Codina RNA journal.

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	3
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	6
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	2
Sous-total personnels non permanents en activité	2
Total personnels	8

EVALUATION

Overall assessment of the team

Scientific production is very good including four original publications, two in very good quality journals (NAR, RNA Biol), and seven collaborative publications, with contributions from all team members. Attractiveness is good (one ANR-DFG). The team had one contract with a private company, and attracted three PhD students, nevertheless visibility and participation to international meetings were rather limited. Outreach of the team is good with limited valorisation and communication to the public.



Strengths and possibilities linked to the context

During the last evaluation period, the team was composed of 1 DR, 1 CR, 3 MC-SU and 1 Al. The team hosted 3 PhD students (1 defended in 2017 and 2 started their PhD in 2021 and in 2022).

The future potential co-PI obtained funding as coordinator: a bilateral French-German ANR-DFG grant, 2021-2025, 190 k€, and a regional grant from the IBPS, 2020-2021, 20 k€.

During the evaluated period, four original research articles were published: three with the current PI as last author (*Biochimie*, 2021; *RNA Biol* 2020; *Oncotarget*, 2018) and one collaborative publication with the potential future co-PI as second to last and co-corresponding author (*NAR*, 2018). In addition, the team published seven other collaborative studies (two co-authored by the current PI and six by the potential future co-PI, most of them with the other potential future co-PI from Collège de France and one with a team from the LBD unit within IBPS).

The team attracted three PhD students over the period, who actively participated in publications: one was 1st author in *RNA Biol* in 2020 and 2nd author in *Oncotarget*, two others were co-authors in one research article and one review.

In total, three articles as 1st author originated from the team, with the CRHC CNRS as first author of the articles published in *Oncotarget*, 2018, and in *Biochimie*, 2021. All members of the team published: the assistant engineer co-authored three publications and two MCU both sign two articles as co-authors.

The future potential PI was editor for a topical collection of the Non-Coding RNA journal.

The team has expertise in polysome profiling and has been collaborating regarding this expertise with many national groups and with the EUKARYS company through a technology support contract that resulted in a publication in NAR in 2019.

Weaknesses and risks linked to the context

The scientific visibility and outreach of the team were limited. Although it attracted PhD students, the team did not attract postdocs. Team members did not attend conferences and received no seminar invitations. They were not involved in public science or evaluation activities.

The future potential co-PI has not published as last author.

Considering the workforce of the team, funding was relatively low over the period.

Analysis of the team's trajectory

The CR CNRS and the current PI of the team will retire in 2024 and the team in its current form will close at the end of this contract. One MCU of the current team and a DR CNRS from another unit will apply to create a new team entitled "Biology of RNA modifications", in the future Dev2A unit at the IBPS. The two future potential co-PIs have been collaborating for years and co-authored five publications in the evaluated period. The current PhD students, the Assistant Engineer and 1 MCU will join the potential new team. The other MCU of the current team will join another Dev2A team.

RECOMMENDATIONS TO THE TEAM

Currently fundings only extends to 2024 and the current team will close at the end of 2024. The potentially new co-Pls should put effort in increasing publications, fundings, visibility (participation to conferences by members of the team), and communications to the general public.



Team 4: Compensation systems in neurodegenerative diseases and ageing

(Brain-C)

Name of the supervisor: Mr Christian Neri

THEMES OF THE TEAM

Team 4 studies the molecular pathways associated with chronic Neuro-Degenerative Disorders (NDD) and their regulation in the brain, mainly focusing in Huntington Disease (HD), but also Alzheimer Disease (AD). To identify these pathways, the team extensively uses a machine-learning driven strategy. In addition, through an innovative cell-biology strategy, the team also studies the role of Small Extracellular Vesicles (SEV) in HD and their potential diagnostic use in AD.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

It was previously recommended that the rate of publication in high profile journals should be increased. During the current period, the team published 13 original research articles (5 as corresponding authors), 5 reviews (1 as corresponding and first author), 34 clinical articles (almost solely authored by 1 researcher from the team). Therefore, the rate of publication in very good journals was stable.

It was also recommended that the team should enhance the number of PhD students and recruit additional researchers. While the team reinforced its permanent staff with two researchers, it did not increase the number of PhDs, and the only PhD student hosted left the lab before completing his/her PhD.

The team was also encouraged to increase interactions with other teams of the unit, but this was not done, at least judging from common publications (only one with the Neurosciences unit at IBPS). Since the PI was the scientific director of the AP-HP/DHU project FAST (Fight Aging & Stress) it is mentioned that collaboration with Team 2 was carried-out in this context but there are not any outcomes mentioned from this collaboration. Operational collaborations with other teams of the unit were also mentioned (maintenance and operation of the human-iPSC core facility of B2A).

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	5
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	4
Post-doctorants	2
Doctorants	0
Sous-total personnels non permanents en activité	6
Total personnels	11



EVALUATION

Overall assessment of the team

Team 4 presents an excellent level of publications (13 papers, four in leading position) in high quality specialty (e.g. ACS Sens., Aging Cell) and more generalist journals (eLife) in leading positions. The attractiveness of the team is very good to excellent in terms of recruitment: seven post-docs were recruited, but only two PhD students. The visibility of the team is excellent, with participation and organization of high-profile conferences (Keystone GRC and EMBO conferences). The team is excellent in raising funds (e.g. CHDI Fondation, ANR-DGOS). The valorisation activity of the team is also excellent with a start-up and one patent filed.

Strengths and possibilities linked to the context

In 2022, permanent staff included two DR, one PUPH one MCF and one IR (one PUPH retired in 2018). Two researchers and four post-docs were recruited during the assessment period, for a total of seven post-docs of which six are foreigners. Of these two left the lab; the others published, but only one as first author. Only two PhD student were hosted during the same period: one did not complete his/her formation, the second one moved to industry.

The team published 13 research articles (four as both first and corresponding, one as corresponding, and eight collaborative), seven reviews (one as corresponding and first author, three collaborative), 34 clinical articles (almost solely by one researcher in the team). Original articles were in high profile journals such as *eLife* and Aging Cell. The PI wrote and published one book (in French). Articles stemming from collaborations appeared in top quality (*Brain, The Nuclei Acids*) or outstanding journals (one *Nature*).

Members of Team 4 were invited to 15 international meetings (EMBO workshops, Gordon Research Conference (GRC) and eight national meetings. They organized two international and four national meetings.

The team leader is the founding Chair of the European-HD Network Working Group 'Systems Modeling' (2008), the HD systems biology consortium initiative 'e-HD' (2022) and the ISEV international Working Group on 'Extracellular Vesicles in the Nervous System' (EVINS) (2023).

During 2017-22 the team raised a total of 2 M€: Five ANRs (three as leader including ANR-DGOS, ANR, ANR/MESRI) and 2 as collaborator; two local grants (SU and SATT Lutech); and 1 grant from charities (CHDI Fondation, USA; 1.4 M€ as leader.

Members of Team 4 appear as Editor-in-Chief, Section Editor-in-Chief and Associate editor.

Team 4 created the start-up BioGemix Pharma, deeptech project in the field of high-end machine learning for optimal disease-target selection, selected by the EIT Health for acceleration. It obtained "maturation" grants by SATT LuTech, CNRS or Sorbonne University and 1 filed patent.

The team is also very active with patient associations (four in total as Association Huntington France (AHF) and European Hematology Association) and gave two interviews (one broadcasted interview by Help4HD international, a UK-based association with mission to educate the world on HD and in Magazine Inserm Science et santé regarding their eLife publication).

Weaknesses and risks linked to the context

Team 4 recruited few PhD students, showing no improvement since the previous evaluation period. Considering that the team has two HDRs, the ratio PhD students/HDR is very weak.

Although the team has an excellent fund-raising track, they did not secure any EU funding, but projects have been submitted (JPND and ERC synergy).

Analysis of the team's trajectory

The team will join the Neuro-SU unit within IBPS at the start of the next 5-year term and their project is therefore described in the Hcéres document of Neuro-SU.



RECOMMENDATIONS TO THE TEAM

The B2A unit will be closed and team 4 will join the unit Neuro-SU at the start of the next 5-year term. It is imperative that the team attracts PhD students and post-docs in the following period to increase its training track record. Effort should be made to establish collaborations with other teams within the future unit. The PI and other researchers should participate in more training networks and could take over more teaching/training responsibilities as a strategy to attract more students. The team should also consider increasing that number of HDRs. The rate of publication of PhD students should also be enhanced. The team should carry on their efforts to attract EU-fundings. More efforts should be made to interact with schools and the general public.



Team 5: Réparation des réseaux neuronaux

Name of the supervisor: Ms Rachel Sherrard

THEMES OF THE TEAM

The team studies neuronal and synaptic development and function, and post-lesion repair of neuronal damage in the context of the ageing brain. It has developed cerebellar and hippocampal models to address the biological basis of these phenomena and to explore clinical applications.

The first axis aims to identify molecules that enable selective synapse stabilization during neural circuit repair, and to discover molecules that enable selective synapse stabilization. The second main axis is based on the effects of non-invasive brain stimulation, using low-intensity repetitive transcranial magnetic stimulation (LI-rTMS) to restore appropriate neuronal connectivity and restore appropriate function.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The recommendations of the previous report were:

- 1- the team should attempt to publish in higher impact journals.
- 2-Team leaders are encouraged to pursue the reorganisation of the team according to research program axes.
- 3- Research strategy is not adequate since team leaders should rapidly focus on the most promising axes.

Point 1: the team improved the quality of publications, notably though internal and external collaborations (ex: Lancet Neurol 2022; Sci Adv 2019; Plos Biol 2018). Overall the team published a large number of articles, reviews and book chapters (52 during the evaluated period).

Points 2 and 3:

Regarding the reorganization of the team, there was no noticeable reduction in the number of research topics. This dispersiveness will hinder the emergence and development of large-scale projects.

The recruitment of a PU-PH in the team should improve interactions with clinicians and clinical studies.

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	3
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	8
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	4
Sous-total personnels non permanents en activité	5
Total personnels	13



EVALUATION

Overall assessment of the team

The scientific production of team 5 is excellent: 52 articles and reviews including 20 original articles in leading position, some in high-ranking journals (for instance in *Sci Adv* and *Plos Biol*). This team has developed potentially cutting-edge research concerning low-intensity repetitive transcranial magnetic stimulation Li-rTMS to improve neuronal function.

Attractivity is excellent: the team trained 9 PhD students and secured important fundings (PI in 1 ANR and coPI in FRM grants). Interactions between basic and clinic research are significant. There is still uncertainty about the sustainability of statutory positions following the upcoming retirements. Outreach is very good with communication to broad audience (for instance article in *Le Monde*).

Strengths and possibilities linked to the context

Team 5 is a dynamic member of the unit with five HDR, six theses defended and three ongoing. It has developed unique expertise in the use low-intensity repetitive transcranial magnetic stimulation (LI-rTMS) to restore neuronal connectivity and function. This is complemented by additional multidisciplinary approaches (electrophysiology, cell biology, animal models,...).

The team regularly publishes in excellent quality journals (Sci Adv 2019; Plos Biol 2018; J Physiol 2022) as first or last author (9 first, 11 last/corresponding), and in excellent journals in collaboration (Lancet Neurol 2022; Nat Comm 2018; Nat Rev Drug Discov 2017). A PUPH in the team has contributed to 11 medical publications (J Gerontol A Biol Sci MedSci; Mov Disord 2022; Plos One 2021). Team members also have contributed to books or book chapters.

The team members have sustained participation in editorial boards (such as *Frontiers in Neuronal Circuits* and *Int J Molecular Sciences*) and numerous national and international scientific assessment activities (USA, Poland, ANR) as well as local grant evaluations. They also have responsibilities in the Conseil National des Universités. Team members are involved in international research networks (ex: Int Brain Stim Conference, Lisbon, 2023).

The team has trained nine PhD students over the last period, including three international students. The team's senior staff has excellent level of involvement in university teaching at both Licence and Masters levels.

The team leader obtained national grants as coordinator (ANR, 2020-2024, 289 k€) or coPI (FRM, 2023-2025, 600 k€) and PhD contracts (such as Labex BioPsy, 2021-2024, 100 k€; France Research on Alzheimer, 2018-2022, 100 k€) allowing appropriate funding for their research projects and the recruitment of PhD students.

Weaknesses and risks linked to the context

Heavy teaching responsibilities may impact research activities, such as grant applications from researchers other than the PI, and technical staff for molecular biology is currently absent. No postdoc during previous period.

As already mentioned in the previous evaluation the large number of research topics pursued by the team leads to dispersion. Focusing on one main axis would facilitate the team's future reorganization and further increase visibility.

Analysis of the team's trajectory

The team will join Dev2A at the start of the next 5-year term, under the team name "Neural adaptation and repair" and their project is therefore described in the Hcéres document of that unit.

RECOMMENDATIONS TO THE TEAM

We advise the team to continue their training activity of thesis students and to try to attract promising young researchers (CR and MCU) to prepare for the next five years-contract. It is recommended that this team pursue recruitment of quality PhD students and postdoc in order to recruit some of them on tenure positions and thus compensate for the upcoming retirements of senior research members of the team.

The team should prioritize key projects and continue the synergy between basic science and clinic.



Team 6: Dynamique de signalisation intracellulaire et

cibles thérapeutiques

Name of the supervisors: Ms Isabelle Limon & Mr Pierre Vincent

THEMES OF THE TEAM

Team 6 resulted from the merge of two previous teams, 'Cellular integration of neuromodulatory processes' and 'Phenotypic control of vascular smooth muscle cells', at the start of the previous contract (in 2017). During the evaluatin period the team focused on understanding the integration process of intracellular signaling (cAMP/cGMP pathways), regulation by phosphodiesterase (PDEs), and its impact in either neuromodulation or vascular function. The ultimate aim was to establish new treatments to limit impact of age on brain or vascular health. Projects included 1) the study of molecular mechanisms involved in phenotype switch in vascular smooth muscle and endothelial cells in different pathological contexts and 2) the development of unique biosensors for detection of very small amounts of cAMP in neuronal population of the striatum.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

"The scientific production is limited"

The two co-Pls published 18 original articles, including two joint papers. However, these publications of the team still have limited visibility. The most cited work is one article in 2017 (*J Physiol*) with 58 citations on the topic of detection of dopamine signalling by FRET biosensors in brain slices.

"Strong relationship with industry vs scientific production of the team"

The contract with Lundbeck biotech has evolved from a service contract to a collaboration leading to a joint publication.

"A clearer program should be built to increase the scientific rationale of the merged groups."

The team has produced two joint publications demonstrating scientific interaction between the two Pls, including one paper in 2018 (Biochim Biophys Acta Mol Cell Res.) on application of biosensor imaging in VSMCs.

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

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



EVALUATION

Overall assessment of the team

The scientific production of the team is very good with nine first/last/corresponding original articles, but these have limited visibility (Biochim Biophys Acta Mol Cell Res, Br J Pharmacol).

Attractivity is very good to excellent. The team obtained funding from caritative associations and Idex, but no ANRs. Two CNRS researchers and one MCU left the team, but involvement in research training was excellent (six PhD students hosted and strong involvement in several Master programs). The team has an international reputation in biosensor design, and helped organize an international conference on this theme. Team members were invited to international meetings (including two Gordon conferences). Valorisation and outreach activities are very good: the team secured industrial collaborations (Lundbeck and Roche, 447 k€) and developed outreach activities with patient association.

Strengths and possibilities linked to the context

During the evaluation period the team was comprised of 6 permanent staff members (one DR CNRS; one PU Sorbonne University; one CR CNRS, three MCU PU Sorbonne University), three of whom hold an HDR.

They recruited four CDD and one postdoc in 2019. Six PhD students defended their thesis during the assessment period, and one PhD student is completing his/her training. The PhD/HDR ratio has ranged from one to four PhD students per HDR, which appears somewhat unbalanced.

Joint scientific production of the two Pls is in specialized journals with limited visibility (Biochim Biophys Acta Mol Cell Res, Br J Pharmacol). Articles in collaboration by either one of the two Pls include Sci Adv, J Cell Sci and J. Physio.

The team's university personnel are heavily involved in teaching, including responsibility in several master programs; one is co-director of the nursing diploma (Advanced Practice nursing diploma, Medical Faculty, Sorbonne).

The team has an international reputation in biosensor design, and participated in organisation of an international conference (International meeting on Biosensors). Team members have been invited to national and international conferences, including Gordon conference, Dopamine 2022, and Molecular Methods in Neurosciences

Team members have collaborated with Teams 2, 5 and 7 members in the unit (4 publications in common).

The team members have been strongly involved in training through research, with co-responsibility for several Masters programs and training of several PhD students and postdocs.

The team obtained funding from National associations (FFC 2017, FdF 2018: = 180 k€), caritative associations (France Parkinson 2017 and 2020; for a total of 88 k€), and from 1 regional excellence fund Idex (Coordinator: REPSELCV 2021 = 64 k€), for a total of 268 k€. The team obtained significant funding from industry (Lundbeck and Roche, 447 k€ in 2019).

Team members have contributed outreach activities including two videos for a youtube channel initiated by RTmfm, réseau de l'imagerie photonique.

Weaknesses and risks linked to the context

The team has not established ANR level national funding or any international funding. No EU level funding was reported.

Their papers have limited visibility (mostly speciality type journals).

At the time of the evaluation, two doctoral students had defended without 1st author publications, although a co-authored manuscript was under revision.

No technical support staff among permanent personnel.

Little clinical (translational) validation and no hospital staff associated with the team.

Analysis of the team's trajectory

Team 6 resulted from the merge of two teams of B2A, 'Cellular integration of neuromodulatory processes' and 'Phenotypic control of vascular smooth muscle cells', at the start of the previous contract (in 2017). The team is now closing, and one of the co-PI has already left the institute.

RECOMMENDATIONS TO THE TEAM

The team will close at the end of this contract. Team 6 will not join the future Dev2A. One of the PIs, together with a MCU, will join another unit at St Antoine, the other one has moved to Montpellier (IGF Montpellier).



Team 7: CARTHER Stem Cells, cardiovascular pathophysiology and biotherapies

Name of the supervisors: Mr Onnik Agbulut & Mr Zhenlin Li

THEMES OF THE TEAM

Team 7 explores the molecular mechanisms underlying cardiovascular diseases development, mainly in an aging-related context, in order to identify and develop new therapeutic strategies. The team has developed approaches focused on stem cells, bio-inspired materials and tissue engineering with the aim of exploring in 3D cell culture and iPSC-derived human cells different cell signaling pathways. The team also studies the molecular mechanisms involved in cardiovascular pathophysiology, in particular on Serum Response Factor (SRF) and its regulated downstream targets. Through collaborative works, Team 7 also investigates the importance of restoring or preventing mitochondrial dysfunction in several pathologies affecting striated muscles.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Previous recommendations.

- The quality of scientific production should be kept.

Team 7 publishes regularly in very good visibility journals. While collaborations resulted in high quality publications, members are rarely in leading position.

- Third party funding should be developed.

Team 7 obtained six grants from national associations/foundations (1 235 k€) and contracts with four biomedical companies (500 k€).

- Closer collaborations within the unit and with clinicians should be envisioned. Translational activities should be improved

Collaborations within the unit appear low with regard to its potential. Absence of PU-PH on the team is noted and members are compelled to collaborate with external clinicians for translational projects.

- The public outreach should be increased.

Several public outreach activities were carried out (popularizing science, general public conferences).

- A mismatch in gender was noted and Team was encouraged to increase the number of females in leading positions.

Team 7 has grown with the addition of five permanent staff; three are women (two CR1 and one IE). Currently, 8/14 members are women.

- The future projects of the former teams should merge in a single "Team project".

Team 7 focused on two axes 'Cardiac remodeling, cytoskeleton and mechano-transduction in cardiac and vascular cells' and 'Cardiac tissue engineering'. These axes are the 'core business' of the two former teams. Some common projects were developed as attested by publications and some co-coordination of scientific grants.

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	3
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	13
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	2
Post-doctorants	3
Doctorants	7
Sous-total personnels non permanents en activité	13
Total personnels	26



EVALUATION

Overall assessment Team 7

The team results from the fusion in 2019 of two previous teams. Its scientific production is very good (31 research articles, 16 reviews in first or leading positions / 88 total papers (*Front Physiol, Sci Rep, ...*). The team showed excellent capacity to obtain national and local grants (four ANR including one as coordinator and two regional funds) and third-party national funding (two AFM-Téléthon, two Fondation de France, two Fédération Française de Cardiologie as coordinator) as well with four private companies.

Valorization and outreach activities were excellent (scientific councils of patient association, and two patents).

Strengths and possibilities linked to the context

Team 7 is currently composed of 14 permanent members (two PU/three MCF, three CR, one DR, two AI/IE, two AJT and one Tech). The publication list reflects a regular and productive scientific production for a team of this size: 88 papers in the evaluation period, including 61 research articles and 27 reviews and one book chapter. Among these, 47 were signed as a first or leading position (30 research articles and 16 reviews). Publications in which team's members are in a leading position are of very good quality (Front Physiol, Sc Reports, Aesthetic Plast Surg, Am J Pathol, Faseb J, Plos One, Int J Mol Sci, F. Cell Dev, Cells). The team was also strongly involved in excellent national and international collaborations (31 papers), enhancing international visibility and the publication record (Nat Com, Circ., Eur Heart Journal, JACC, EMBO J, Circ Res).

As major scientific results, Team 7 highlighted the role of two transcription factors, Serum Response Factor (SRF) and Bcl11b, in vascular or cardiac remodeling. Team 7 is also involved in several collaborative projects to optimize and develop cardiac cell/mitochondrial/vesicle therapy. They designed human cardiomyocytes derived from iPSCs and derivatives (secretome, extracellular vesicles, mitochondria) and developed different biomimetic biomaterials for cardiac or skeletal tissue engineering. Team also conducted excellent valorisation activities and collaborated with several private partners to generate 2D and 3D cell culture in a new iPSC technical facility and related tools to explore disease mechanisms and to perform drug testing.

Team 7 obtained grants from national agencies (four ANR including one as coordinator), and regional/local sources: two Gérond'if DIMs as coordinator, two Sorbonne University grants). Team 7 also obtained six grants from national associations and foundations (two AFM-Téléthon, two Fondation de France, two Fédération Française de Cardiologie as coordinator) and has contracts with four biomedical companies (Capstan Therapeutics, Ksilink etc). Altogether, team 7 obtained 2 600 k€ (excluding recurrent institutional funding).

The team showed an excellent attractivity and ability to recruit and train PhD students. Since 2017, 10 PhD students from the team have defended their thesis (only 1 without 1st author publications yet), and five others are in mid-term (linked to four HDR). Attractivity of PhD student could be related to the strong involvement of the team in teaching activity and excellent outreach activity (responsibilities of teaching units, member of 'Integrative Biology & Physiology department of Sorbonne University, involvement in public conferences etc). Team 7 also benefited from SU Idex or IBPS sponsored incentive actions or joint PhD students for interdisciplinary PhD program. Team 7 also hosted 10 post-doctoral researchers, 4/10 of whom have published as first author.

Weaknesses and risks linked to the context

Several members of the team could potentially leave or retire during the next contract (one PREM, one PR, two CR1, one IE), so that starting in 2026 the team could be composed of only six researchers (one PU, one DR, one CR, three MCF) with a limited number of HDR. Similarly, the recent departure of two technical staff (one IE Inserm in 2019, one IJT/ATFR not mentioned currently) is noted, with another two technical staff to retire soon (one IE CNRS in 2024, and one CNRS Technician currently). The technical permanent staff will thus soon be down to one IE CNRS and one university AJT. In addition, the team seems to have had difficulty in recruiting new young permanent researchers, since the new arrivals during the evaluated period result from the mobility of established researchers. In addition, the absence of clinician on the team may limit translational research, and the leadership in clinical/translational articles.

The team's participation in European networks is limited to scientific collaborations, with no recent European grant fundings. Moreover, only the team's co-headers are currently involved in grant applications. The same applies to the organization of scientific events, and responsibilities on various boards and academics local or National councils. This could reduce the visibility of junior or mid-career members of the team.



Moreover, it is noted that although several collaborative papers are published in excellent journal (Nat Com, Circ., Eur Heart Journal, JACC, EMBO J, Circ Res), team members are not present in leading positions.

Analysis of the team's trajectory

For the next contract, team 7 will join the new research unit Dev2A. The team will remain focused on the understanding of cardiovascular remodelling in age- and disease-related heart failure devoting attention to cytoskeleton organization and mechanotransduction pathways in order to be develop new therapeutics to counteract their progression. Team will continue to develop and use innovative cell and tissue models and their associated analysis tools. The team's project appears to fit into one thematic axe of the future unit: Stem cells, differentiation and regeneration.

RECOMMENDATIONS TO THE TEAM

The "Biological Adaptation and Ageing" unit will be closed and Team will join the future Dev2A. As global recommendations, recruitment of additional young researchers or PH/MCF would be required to ensure the stability of research lines for the future. With the future retirement of permanent staff, it would be recommended for the team to promote over the next term obtention of the HDR diploma among their current MCF staff. Additionally, discussions of strategies to increase/maintain the number of technical support staff, notably for bioinformatics, would be useful.



Team 8: Epigenetics and RNA metabolism in human diseases, EpiRNA

Name of the supervisor: Mr Christian Muchardt

THEMES OF THE TEAM

The team works on the function and regulation of "RNA-byproducts" of gene expression, i.e., intronic, read-through or promoter- and enhancer- associated RNAs, which are rich in repeated sequences, including retrotransposon-derived sequences. The team has a special interest in studying the co-transcriptional events occurring on chromatin linked to the production of these RNAs. Repeat-rich intronic or intergenic RNAs may fold into double-stranded structures and favour inflammation by triggering anti-viral defence mechanisms. Moreover, toxic spliced variants may be produced via deregulation of accurate splicing. As such, the team has strong focus in studying the deregulation and the involvement of processes linked to the production of RNA-byproducts in inflammatory diseases and aging.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous Hcéres committee recommended to publish three pre-prints in peer-reviewed journals. One paper, signed as 1st author by a PhD student who defended in 2019, is mentioned as still unpublished in a peer-reviewed journal.

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

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

EVALUATION

Overall assessment of the team

Scientific production was excellent: five original research articles as leader in high-quality journals (for example EMBO J, two NAR). Attractiveness of the team was very good to excellent. The team secured continuous financial support from national public grants (Plan Cancer, INCa and Labex as coordinator, three ANR as partner). Three PhD students and two postdocs were recruited, but half of them have not published as first author. PI gave oral presentations at two international conference (EMBL, RNAMeeting). Outreach activities were very good but restricted to PI (participation to festival linking science to art).

Strengths and possibilities linked to the context

During the last period, the team was composed of one DR, three CR (one left in 2020), 2 CDD bioinformaticians and two technicians from the Pasteur Institute until 2022. The team also hosted two postdocs and three PhD students (two defended).



The team obtained more than 0.6 million Euros during the period from national public grants (Plan Cancer and INCa as the coordinator, three ANR as partner) and one Labex, allowing the salary of a bioinformatician for most of the period. Two contracts continue until end 2024 (Labex and INCa). All permanent members of the team are actively involved in fundraising.

Original research from the team led to 5 publications with the PI of the team as last author in high-quality journals (EMBO Rep, 2021; EMBO J, 2019; LSA, 2021; NAR, 2021 & 2022). During the period, three of these publications have a PhD student and/or a postdoc or a bioinformatician as first author. The other two articles are each signed by one of the two CR as first author. Collaborative work includes two Nat. Comm, one signed second-to-last and one signed as last author by a CR who left the team in 2020.

The team attracted three PhD students, two postdocs and one visiting PhD for three months. One PhD student in another institute was co-directed by the PI and published as 1st author in Viruses, the PI signing this publication just before the last author.

During the period, the PI of the team had four oral communications in international conferences, including one symposium in Denmark as an invited speaker. The PI has been expert for the Hcéres, member of the ARC national commission and is deputy director of the INSB since 2020.

The PI published one chapter book and contributed to public science during a festival in Denmark linking Art and Science.

Weaknesses and risks linked to the context

Only half of the defended PhD students and postdocs hosted in the team published as 1st author. Indeed, during the period, two PhD students defended in 2019, and two postdocs were hosted for two to three years each (2019-2020 and 2021-2023). One PhD student and one postdoc are co-first authors of one publication in LSA in 2021. However, the other PhD student (with one manuscript in Biorxiv) did not publish as 1st author in a peer-reviewed journal yet, and the other postdoc did not publish yet as first author.

Except for the PI of the team, there is no mention of participation to meetings, public science or evaluation activities for other members of the team.

The PI of the team mentioned the lack of wet-lab technical assistance since the end of technician contracts from the Pasteur Institute in 2022.

The team joined B2A in 2020. No publication has yet originated from collaboration with other B2A teams.

Analysis of the team's trajectory

Over the past years, the team had more focus on genomic approaches and, it makes sense that the team wishes to join the LCQB unit within the IBPS after the closure of B2A. All three permanent members of the team will be present for the next contract.

RECOMMENDATIONS TO THE TEAM

An effort in consistently involving PhD and postdocs as first authors needs to be done, perhaps by implicating more closely all the CR of the team in student supervision. The committee recommends that all the PhD students and postdocs who have been hosted in the team during the evaluated period sign at least one publication as first author. For those who have left the team, their projects are to be continued and finalized by current members of the team.

It should be considered that all members of the team contribute in the scientific visibility of the team, e.g., by participating to meetings and public science outreach.

As all the technical staff contracts ended and the current funding grants will end after 2024, technical and financial support needs to be secured for the next period.



CONDUCT OF THE INTERVIEWS

Day 1, Wed. October 4

10h00-11h00 arrival, closed door meeting of committee room B501

11h00-11h15 presentation of the committee

11h15-11h55 Presentation by the director, open to all the Unit

(20 minutes presentation, 20 minutes questions)

coffee available

team presentations (50 min each)

11h55-12h45 **Team 1** Margaret AHMAD

(15 min presentation, 15 min questions; 5 min PI alone with committee; 15 min closed

door debriefing of committee)

12h45-14h00 packed lunch

14h00-14h50 **Team 2** Bertrand FRIGUET

14h50-15h40 **Team 3** Olivier JEAN JEAN

15h40-16h30 **Team 4** Christian NERI

16h30-17h20 **Team 5** Rachel SHERRARD

17h20-18h10 **Team 6** Isabelle LIMON / Pierre VINCENT

18h10-19h00 committee debrief of the day

End of all sessions

Back to hotel (or check-in)

Dinner

Day 2, Thurs. October 5

8h30-9h00 arrival of committee/coffee

9h00-9h50 **Team 7** Onnik AGBULUT/ Zhenlin LI

9h50-10h40 **Team 8** Christian MUCHARDT

10h45-11h15 Discussion with docs and post-docs

Representatives: Tania Medali and Mélanie Bezard

11h15-11h45 Discussion with Scientists (researchers other than team leaders)

Representatives: Eric Batsché and Liliana Castro

11h45-12h15 Discussion with support staff (technical and administrative personnel)

Representatives: Mohamed Doulazmi and Aurélie Prats

12h15-13h30 packed lunch; debriefing of committee

13h30-14h00 Meeting with the managing bodies

Yvan de Launoit (DAS) et Carina Prip-Buus (DS), CNRS INSB, Section 24

Camille Chaudonneret et Karine Lanini, Inserm

Elisabeth Angel-Perez, Vice-Présidente Recherche et Innovation,

Philippe Agard, Vice-doyen Recherche de la Faculté de Science et Ingénierie

14h00-14h30 Closed door meeting of committee (in presence of the Hcéres scientific advisor)

14h30-15h15 Discussion with the directors

15h15-17h15 Final debriefing with snacks and drinks



GENERAL OBSERVATIONS OF THE SUPERVISORS



Marie-Aude Vitrani Vice-Présidente Vie institutionnelle et démarche participative Sorbonne Université

à

Monsieur Eric 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

Paris, le 13 décembre 2023

Objet: Rapport d'évaluation - DER-PUR250024366 - B2A - Adaptation biologique et vieillissement.

Cher Collègue,

Sorbonne Université vous remercie ainsi que tous les membres du comité HCERES pour le travail d'expertise réalisé sur l'unité de recherche « B2A ».

Sorbonne Université n'a aucune observation de portée générale à formuler sur le rapport d'évaluation transmis.

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

Marie-Aude Vitrani Vice-Présidente Vie institutionnelle

et démarche participative

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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