Research evaluation

EVALUATION REPORT OF THE UNIT

RID-Age - Facteurs de risques et déterminants moléculaires des maladies liées au vieillissement

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Université de Lille,
Centre hospitalier régional et universitaire de Lille - CHRU Lille,
Institut national de la santé et de la recherche médicale - Inserm,
Institut Pasteur de Lille

EVALUATION CAMPAIGN 2024-2025
GROUP E

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High Council for evaluation of research and highter education

In the name of the expert committee :

Muriel Laffargue, chairwoman of the committee

For the Hcéres :

Coralie Chevalier, president

In accordance with articles R. 114-15 and R. 114-10 of the Research Code, the evaluation reports drawn up by the expert committees are signed by the chairmen of these committees and countersigned by the president of Hcéres.

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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Mr Hugues Lortat-Jacob, INSB CNRS
Mr Dominique Lacroix, Dean of the UFR3S, Université de Lille
Mr Benoît Robyns, VP research, JUNIA, Lille

CHARACTERISATION OF THE UNIT

- Name: Facteurs de risques et déterminants moléculaires des maladies liées au vieillissement
- Acronym: RID-Age
- Label and number: U1167
- Composition of the executive team: Philippe Amouyel

SCIENTIFIC PANELS OF THE UNIT

SVE
SVE 6

THEMES OF THE UNIT

UMR1167 is dedicated to the identification of aging-related diseases and the study of their impact on healthy life expectancy. Research objectives are to identify determinants that can be acted upon in order to treat chronic pathologies such as cardiac disease, Alzheimer and, with the arrival of a new team in 2022, metabolic diseases. The unit's expertise is complemented by teams specialising in epidemiology and biochemical mechanisms associated with aging.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The UMR 1167 was created in 2015 from the UMR744 'Public Health and Molecular Epidemiology of Aging-Related diseases' initially created in 2006 and renewed in 2010. UMR1167 is distributed on three distinct research campuses. Teams 1, 2 and 3 are located at the Institut Pasteur de Lille (IPL), team 4 at the Haute-Borne CNRS Campus (with part of the NMR facility at IPL), teams 5 and 6 at the UFR3S (Health campus, CHU Lille & Lille University).

RESEARCH ENVIRONMENT OF THE UNIT

UMR1167 is under the supervision of multiple institutions: University of Lille, Inserm, CNRS (one team), Institut Pasteur de Lille (IPL) and Lille University Hospital (CHU Lille).
UMR1167 benefits from the research supports available on the three campuses (IPL, University Health Campus and CNRS), as well as from the different supervisory bodies. In 2012 UMR1167 obtained the label laboratory of Excellence (Labex, PIA) Distalz 'Development of Innovative Strategies for a Transdisciplinary approach to ALZheimer's disease' that was extended for 6 additional years in 2020. This Labex, together with other PIAs of the Hauts-de-France Région, supported the structuration of the 'Precision Human Health' hub of the I-SITE (Initiatives for Science, Innovation, Territories and Economy) ULNE (PIA) created in 2020. UMR1167 is eligible for all of the calls and animations organised by the I-SITE. By virtue of its affiliation with Lille University, UMR1167 is also integrated within the Public Experimental Establishment (EPE).

UNIT WORKFORCE: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	12
Maîtres de conférences et assimilés	14
Directeurs de recherche et assimilés	8
Chargés de recherche et assimilés	7
Personnels d'appui à la recherche	31
Sous-total personnels permanents en activité	**72**
Enseignants-chercheurs et chercheurs non permanents et assimilés	7
Personnels d'appui non permanents	15
Post-doctorants	12
Doctorants	19
Sous-total personnels non permanents en activité	**53**
Total personnels	**125**

DISTRIBUTION OF THE UNIT'S PERMANENTS BY EMPLOYER: in physical persons at 31/12/2023. Non-tutorship employers are grouped under the heading 'others'.

Nom de l'employeur	EC	C	PAR
INST PASTEUR LILLE	0	2	17
U LILLE	14	0	4
AUTRES	4	7	6
CHRU LILLE	8	0	3
Inserm	0	6	1
Total personnels	**26**	**15**	**31**

GLOBAL ASSESSMENT

The RID-Age unit (Risk factors and molecular determinants of aging-related disease), UMR1167 is distributed on three distinct research campuses located at the Institut Pasteur de Lille (IPL), the Haute-Borne CNRS Campus and the UFR3S (Health campus, CHU Lille & U Lille). The unit develops innovative and competitive research projects in the field of aging. Its aim is to identify determinants of age-related diseases such as vascular and neurodegenerative diseases, and study them through multidisciplinary approaches including population epidemiology, structural biology, and molecular and cellular studies of pathophysiological pathways underlying these diseases.
Significant findings of the laboratory include the identification of biomarkers in age-related diseases, the discovery of novel genetic variants of Alzeihmer disease, and the identification of prognostic indicators of fatal cardiovascular events. Overall, the level of publication of the unit is excellent in relation to its size and financial resources. Ridage members published 441 original articles over the 2018–2023 period, including 40% signed as leading authors, with articles in first-class generalist and specialised journals such as Nature genetics, Angewandte Chemie, Chest, Kidney International, Cell death and Diseases, and Cell Reports. Their publications led them to participate to national and international congress as invited speakers (Alzheimer EuropeConference, European Academy of Neurology, South Texas Alzheimer's conference, International Symposium on Advances in Analytical Pharmaceutical Analysis…) reflecting their excellent international visibility which is even remarkable for the unit's current director. The unit showed remarkable fundraising capabilities. Over the assessment period, it secured 26 competitive European grants (H2020 Costream, ANR-

ERA-net JPcofund PGM-AD, ..), 26 ANR-backed projects (12 as coordinator), 31 contracts from national associations and foundations (Fondation de France, 3xFederation Francaise de Cardiologie, 3xFrance Alzeihmer ..), and two labelled Equipe FRM, for a total of 27.8 M€. The unit's attractiveness is also reflected in its successful recruitment of eight researchers (4 CRCN and 4 MCU/PH). Training over the past mandate was very good: 38 PhDs were recruited and trained during the 2018-2023 period and fifteen postdoctoral fellowships were obtained.
RIDAge Equipment and platforms including LC-MS/MS, mitochondrial high resolution respiratory analyser, NMR platform, Biological resources (CRB) and supercritical fluid chromatography (SFC) certified and labelled, ensure strong ties to Lille university and quality research. Societal impact of the unit is overall excellent. This is evidenced by their strong involvement in international consortia (notably the cardiovascular Risk consortium (NEJM, 2023), and several large epidemiological studies backed with the biological resource centre, six patents and several industrial contract (AstraZeneca and Taros Chemicals Germany, Sanofi, AptamiR...). Some of the unit's members also played a major role in publicising the project in the media (Le Figaro, JDD, Le Parisien, Télématin, La Voix du Nord, L'Express and Radio France).
The centre could attain its full potential by concentrating human resources on the same site and acquiring a shared lab manager. The unit would also benefit from a scientific steering committee to organise scientific events such as a scientific retreat. The upcoming mandate is pivotal to consolidate communication between the three teams of the future unit. The ability to maintain a balance between research on neurodegenerative and cardiometabolic diseases, basic and translational/valorisation projects, will contribute to affirming the identity of Ridage in its ecosystem (i.e. age-related diseases). The implementation of a scientific advisory board could consolidate the impact of their distinctive strategies. Overall Ridage was assessed as an excellent Unit.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The unit broadly followed the recommendations of the previous report. While it increased the number of HDRs, the number of PhDs remains low. UMR1167 obtained two CRCN positions from the Inserm and the CNRS, a tenure-track IPL position, and a research associate professor position during the contract. A formal 'règlement interieur' and a laboratory council were established. An effort was made to facilitate integration of foreign students by accompanying them through the administrative complexities. Interactions between the five teams were improved, as demonstrated by the publication of 46 common articles and the co-supervision of two PhD students by different teams.

B - EVALUATION AREAS

Guidelines for all areas of evaluation (1, 2, 3 and 4): Considering the references defined in the unit's evaluation guidelines, the committee ensures that a distinction is made on the outstanding elements for strengths or weaknesses. Each point is documented by observable facts including the elements from the portfolio. The committee assesses if the unit's results are consistent with its activity profile.

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

Assessment on the scientific objectives of the unit

The scientific objectives of the unit are excellent. They develop innovative and competitive research projects in the field of aging, with the aim of identifying and analysing the impact of age-related diseases such as vascular and neurodegenerative diseases. To achieve this goal, they combine multidisciplinary approaches such as population epidemiology of age-related diseases, structural biology, and molecular and cellular studies of pathophysiological pathways underlying these diseases.

Assessment on the unit's resources

The unit's resources are outstanding with a total budget of 27 M€ obtained from national and European grants (among them, 15 EU contracts with 7 as PI, 12 ANR grants 6 as PI and 2 Equipes FRM obtained during the 2018–2023 period). They recruited during the contract seven permanent positions (3CRCN, 2 MCU, 2 MCU-PH) and four permanent engineers and three permanent technicians.

Assessment on the functioning of the unit

The functioning of the unit is overall excellent with a full adherence to human resources, Safety, and Health & Safety rules.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

Ridage develops innovative and competitive research projects in the field of aging through the study of age-related vascular and neurodegenerative diseases. They combine multidisciplinary approaches including population epidemiology of age-related diseases, structural biology, and molecular and cellular studies of the pathophysiological pathways underlying these diseases. From this knowledge, they aim to identify novel determinants to treat and prevent aging-related pathologies, thereby increasing healthy lifespan.
These objectives are in line with the guidelines set by national and local supervisory authorities, in particular the IPL scientific strategy of 'Vivre mieux, plus longtemps'. UMR1167 is an important element in the structuring of the University of Lille and a key actor within the framework of the 'Precision Medicine Health' hub of excellence.

Weaknesses and risks linked to the context

The diversity of themes is a weakness given the size of the unit.

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

The unit relies on staff of 128 collaborators, including 41 permanent researchers, fourteen postdoctoral fellows, 45 engineers and technicians (12 under temporary contracts), 21 PhD students and three administrative staff. The unit recruited eight permanent researchers, four permanent engineers and three permanent technicians during the contract. Over the past six years, the unit's budget was 27,308 k€ (including 5,688 k€ recurrent funding from the governing institutions (Inserm, University , CNRS, IPL, CHRU). Resources increased yearly (from 3,700 k€ in 2018 to 5, 462 k€ in 2023).

Weaknesses and risks linked to the context

No major weakness detected

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

UMR 1167 adheres to human resource regulations concerning gender equality and discrimination. The overall gender ratio is balanced (69 women to 59 men), with a slightly higher number of men among the researchers

(29 men to 15 women). The life of the unit is well structured with a welcome day for new members, weekly meetings, and an annual general assembly (AG). Professional development is highly supported and successful in promoting career promotions. The unit should also consider the evolution of personnel in 'lab manager' positions and devise specific strategies for career development and promotion. Lastly, the unit should address the increased administrative workload, as it may affect the research activities of the staff.
The unit has implemented a formal 'réglement intérieur' and a laboratory council, comprising principal investigators and elected representatives, which convenes at least once a year. Health and safety protocols, including those addressing psychosocial risks, are well established. Prevention officers manage biological risks, and new unit members receive specific training. There are specialised procedures for handling GMOs and animal models. To safeguard scientific data, the unit's IT and networks are secured with multiple firewalls, antivirus software, and daily backups. The unit is also committed to minimising its environmental impact, promoting recycling, reducing its carbon footprint, and conserving energy for a greener campus. Technical platforms are supported by adequate staff.

Weaknesses and risks linked to the context

The lack of biostatistician engineers is a limitation considering the increasing quantity of data generated.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The attractiveness of the unit is overall excellent. In addition to recurrent funding (approx. 5.7M€), the unit obtained numerous additional competitive grants as PI or partner (> 70, approx. 21.6M€) including international grants (2xUS Alzheimer Association, JP co-fuND2, ITN, Interreg NWE Regenertis, for a total of approx. 4.1M€), national PIA grants (Labex PIA-Distalz/ FHU/RHU)/ANR/2xFRM team/CPER/CP'Mosaix' (approx. 14.1M€), regional grants (approx. 2.8M€) and ten industrial grants (approx 0.6M€). Over the evaluation period, the Unit had a good record for recruitment of researchers (7 permanent positions and 14 postdocs), and 38 PhD students, demonstrating its competitive position. Members of the units have been initiated in international and national meetings (>100) and some of them are part of national steering bodies (Inserm, CNRS, SFN, …).

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

Ridage team members were invited to national and international meetings, including prestigious ones (e.g. Alzheimer meeting, ATHERONET, ESC, Printemps de la Cardiologie, COST CARDIORNA, Fondation Lefoulon Delalande, Amyloid International Conference, EuroTau meeting, ISMAR, EUROMAR and other workshops). They participated to over one hundred international conferences and 197 seminars and oral presentations. Ridage team members were part of the organising committees of more than fifteen national and international congresses (Webinars for Alzheimer, network F-CRIN INI-CRCT, annual EADB consortium, GERM meetings, Annual EUGMS session). Senior researchers act as editorial board members of European and American organisation and journals in the fields of ageing, neurodegenerative disease and cardio metabolism (general director Fondation Alzheimer, SFGG, EUGMS, Nutrients...). Unit members are represented in national scientific councils (SFN, MRC UK, IPL, Int Master, Faculty of pharmacy UFR3S, University Lille), steering research committees and national instances (Inserm, Hcéres, ANR or ANRS, CoNRS20).

Ridage hosted 5–10 scientific and medical master students every year. The unit hosted 13 visiting PhD students/postdoctoral fellows from Austria, Belgium, Germany, Greece, Italy, Poland, Portugal, Serbia, Spain and the UK. Students integrated teams according to the rules of the Doctoral School (maximum of 3 PhD thesis students per HDR). With the exception of the Covid crisis period (2020–2022), the unit organised a yearly social outing and an IPL campus day. The unit had a high success rate in obtaining masters and doctoral grants from the regional councils of Lille University, Inserm, IPL, CHR, the MESRI and the I-SITE.
The unit recruited three CRCN, two MCU, two MCU-PH, four technicians. It supported members in the application process for new positions or promotions (2 DR2 to DR1, 2 CRCN to DR2, 3 CRCN to CRCH, 2 MCU to PU). Six engineers/technicians were also promoted at different levels (IPL, Inserm, CNRS and UNIV LILLE). A welcome program facilitates integration of new personnel, including administrative support by the Institut Pasteur Lille, University of Lille or CNRS for foreign visitors. The unit works on cohesion with weekly meetings of the whole unit to discuss projects and organises an annual social event.

During this contract, the success rate to various international and national calls increased: at the international level, teams were coordinators of one European JPND JP-cofuND2, UEFISCDI Repair 2training networks (Cofund Marie Sklodowska-Curie Actions and MSCA doctoral network), and partners in six other projects: *CSA* European Brain Research Area, ERA4Health Cardinnov, 2 ANR-ERA-net JPcofund, Interreg NWE, EJPRD JTC 2022. One team (team 3) obtained two funding from the Alzheimer Association USA. At the national level, two teams obtained competitive FRM labelling support, and all teams obtained a competitive national grant during the mandate with a total of 26 ANR-funded grants (12 as PI, 14 as partner), 8 private association grants (Fédération Française

de Cardiologie, Fondation de France, Fondation Cœur et Recherche, Fondation recherche Alzheimer, ESFD). Three teams are part of a Programme d'Investissement d'Avenir PIA (Labex Distalz as PI (3.5 M€), RHU AS-STOP as member (500k€), FHU Carnaval and Remod-HF as a member (80k€ as a member).

Ridage has integrated preclinical models (animal housing facilities), Drosophila and C. elegans facilities unique in the Haut-de-France region and mutualised several platforms. These include: 1) a biological Resources Centre (CRB-IPL) managed by team 1 (thousands of biological samples certified to the NF S96-900 standard), 2) a NMR platform coordinated by team 4 (National Infrastructure Infranalytics), 3) Olink signature platform operated by team 2 (1 IE Univ Lille and 1 AI, IPL), 4) a Bicel platform as part of UMS PLBS (confocal and spinning disk microscopes), 5) a high content screening platform (RTCA ICELLIGENCE instrument, mitochondrial high-resolution respirometry analyser, real-time oxygen cell consumption analyser.). Additional shared equipment includes a LC-MS/MS, a Supercritical fluid chromatography (SFC), a Binding platform and the University Computing Centre.

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

The level of attractiveness is not even between teams: participation as board members of organisations or journals is only ensured by members of three teams. The number of PhD students who plan to perform postdoctoral studies is low, which ultimately affects the capacity of Ridage to recruit young researchers in the future. While technical support is provided for the CRB-IPL, the NMR, the Olink and the BiCell platforms, there is currently no permanent technical staff dedicated to other platforms. Training and maintenance of equipment are the responsibility of a contact person (usually the principal user), which may impact their research activities. Team 4 will not be part of the next renewal, which may have a negative impact on billing for service.
The number of current doctoral students (17) is below the number of HDRs (38 in total, of which 11 defended recently).

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The scientific production of the unit is excellent, with groundbreaking discoveries in age-related neurodegerative disorders and cardiovascular diseases, including the discovery of novel genetic determinants of Alzeihmer disease (Nature Genetics 2022), and identification of novel biomarkers of cardiovascular diseases (Circ Heart Fail, 2018).

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

The unit published 441 articles related to its main research activities in peer review journals, including 169 in leading position in top journals. These include a Nature Genetics in which they published the discovery of a novel determinant of Alzheimer diseases, Angewandte Chemie, Chest, Kidney International, Cell Death and Diseases, and Cell Reports.
The number of publications correlates reasonably well with the size of the team. Three teams published 65 articles each, one published 177 articles (70 of which are consortium papers) and 2 teams published 45 and 26 articles each. Most publications are co-authored by several members of the unit, and all support staff is associated with publications. Students who defended their thesis during the evaluation period published an average of 3.5 article associated with their thesis work.

The scientific production of the unit complies with the principles of research integrity, ethics and open science. The unit complies to all Ethical and regulatory rules (including GDPR and regulations regarding human and

animal research). The unit takes special precautions regarding animal research with all studies being pre-approved and conducted in accordance with the Animal Care and Use Ethics Committee and the need to have a level 1 animal use authorisation or a dedicated training before manipulating animals. PhD students are trained to scientific integrity by the doctoral school. An electronic lab notebook is being implemented in the different teams concerned. The unit complies with open science principles: all articles are deposited on the HAL repository and a majority of articles are available on open access. Summary statistics or even raw data related to omics are made available publicly available through repositories.

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

The number of publications in leading generalist journals is low.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

Societal impact of the unit is overall excellent. This is evidenced by their strong involvement in international consortia (notably the cardiovascular Risk consortium (NEJM, 2023), and several large epidemiological studies backed with the biological resource centre, six patents and several industrial contracts (AstraZeneca and Taros Chemicals Germany, AptamiR...). Some of the unit's members also played a major role in publicising the project in high-profile media.

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

The unit's non-academic collaborations include the development of innovative biomarker discovery and therapeutic strategies in the domains of aging-related disease, cardiovascular and neurodegenerative diseases, diabetes, and epidemiology. These partnerships have been reinforced through exceptional collaborations with Sanofi, Astra Zeneca, as well as the smallest structures such as Genoscreen and Hybrigenics. This has resulted in the filing of six patents, of which three with the JUNIA School of Engineering. Several teams have actively engaged in maturation and pre-maturation projects in collaboration with SATT Nord, Eurasanté and Inserm Transfer. One project was integrated into the bio incubator Eurasanté (Tau immune), and one Contrat de plan Etat-Régions (CPER 'longevity') was obtained. One team patented a Patent Nanobody Z70. One team established the prevention program Tempoforme, which collects data and samples to examine biomarkers of aging. The unit's research has also led to the development of numerous epidemiological studies, new processes and products with potential clinical applications.
The unit is deeply committed to research dissemination, bridging the gap between science and society through various initiatives. They actively engage with the regional and national press, radio, and TV programs to discuss their research and international collaborations. Social media is also leveraged to communicate their activities.
Communication strategies include initiatives to improve disability-free life duration, promote prevention (Covid epidemic), and advance personalised medicine. They have published comics explaining the impact of DTC genetic tests, created a guide for Alzheimer's prevention, and launched the 'je décide de bien vieillir' initiative.
The unit staff participates in teaching/training mainly for License and Master as well as for secondary and high school students.
The unit organises visits, conferences, and specific events for patients and their families to discuss new treatments and therapeutic strategies.

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

There is a lack of a 'Programme hospitalier de recherche clinique' (PHRC)
The unit has no clinic trials.

ANALYSIS OF THE UNIT'S TRAJECTORY

Over the past ten years, UMR1167 has developed an overarching research project aimed to identify and analyse the complexity and impact of the main aging-related diseases on healthy life expectancy. The trajectory of the unit for the next mandate (2026–2030) is linear in terms of scientific objectives, and overall excellent, with some restructuring: three well-balanced teams with strong scientific objectives will refocus in a single workspace renamed: 'Integrative epidemiological and molecular approaches to improve aging-related chronic disease understanding'. This renaming of the unit reflects the need to address the complexity of aging-related diseases.

During the last mandate, three teams (4, 5, 6) joined Ridage. For the next mandate, team 4 (Integrative structural biology), currently located at the Haute-Borne CNRS campus (with part of the NMR facility at IPL) will create a new single team research unit, as requested by the CNRS. Team 5 (Glycation, from inflammation to aging) will also create its own single team research unit. This, together with the retirement of several researchers and the departure of the director of team 1, opened up new opportunities for the reorganisation and re-centring on the original and ambitious project developed by the three remaining teams in a new entity. Team 1, now headed by a former member of the team and comprised of a total staff of nineteen, will focus on' Vulnerability factors in aging-related diseases', including cardiovascular and cerebrovascular pathologies, chronic kidney disease, and subsequent cognitive decline; Team 2, will arise from the merging of teams 2 and 6 and will be headed by a former member of Team 6. It will be comprised of a staff of ten and focus on 'Molecular and cellular pathophysiology of cardiometabolic diseases'. Team 3 will continue focusing on 'Molecular determinants of Alzheimer's disease and related disorders' under the same direction and a staff of thirteen. The three constituent teams will benefit from strong scientific interactions and complementarity. For instance, team 1 will develop a continuum with team 3 with research on cognitive decline, and make its expertise on new AI and deep learning approaches available to the other two teams. Team 2 will contribute its expertise in epigenetic remodelling and analysis and will develop in vitro models with team 3. Team 3 will develop strong interactions with teams 1 and 2 at methodological, technological and scientific levels.

The restructuring will unite three Ridage teams on a single research campus (September 2024). Potential pitfalls include a time-consuming move, loss of an institutional partner with the departure of team 4; support from Lille University without being located at the UFR3S (Health campus = CHU Lille & U Lille). In summary, the downsizing and relocation of the unit may result in both positive and negative outcomes, refocusing research on complementary objectives, but requiring important efforts to maintain national and international competitiveness and permanent positions for platforms and unit management.

RECOMMENDATIONS TO THE UNIT

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

The committee recommends that exchanges between teams be maintained in order to increase the number of joint projects.

Recommendations regarding the Evaluation Area 2: Attractiveness

The research projects developed by two teams will not be pursued in the next mandate. The remaining three teams need to continue securing competitive funding, especially European research programs. Remaining teams should continue their participation in bodies for steering research or scientific expertise.

Recommendations regarding Evaluation Area 3: Scientific Production

The committee recommends increasing the number of publications in top-level generalist journals.

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

The committee recommends maintaining their contribution of research activities to society. In view of the themes developed, the development of clinical trials could be encouraged by PHRCs, for example.

TEAM-BY-TEAM ASSESSMENT

Team 1: Public health and molecular epidemiology of age-related diseases

Name of the supervisor: Ms Aline Meirhaeghe

THEMES OF THE TEAM

The research program is dedicated to the analysis of risk factors including genetic and environmental factors and molecular determinants of cardiovascular and cerebrovascular diseases that increase with aging and their link with brain aging. The team particularly focuses on acute coronary syndrome, stroke, Alzheimer's disease and more recently developed a topic related to chronic kidney diseases thanks to the recruitment of a new researcher on this topic, and because chronic kidney diseases share common risk factors with cardiovascular diseases. Over the past contact, the team developed five interrelated research topics: 1) acute coronary syndrome, stroke and their link with brain ageing; 2) assessment of genetic susceptibility to cardiovascular and neurodegenerative diseases; 3) participation in international consortium on prevention; 4) the role of environmental risk factors in the development of cardiovascular diseases or their risk factors and 5) determinants and prognosis of chronic kidney disease.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team followed recommendations from the previous evaluation. In particular, they trained 6 members to the use of the French medico-administrative database (Système National des données de santé) and they developed their expertise in environmental factors. They attracted PhD students and post-doc scientists as well as a non-permanent statistical engineer and a physician specialised in electronic medical records. The number of PhD students remains low with respect to the total number of HDRs. As suggested during the previous evaluation, the important number of consortia in which team members participate is an opportunity to exchange young researchers and attract visiting researchers or postdoctoral scientists.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	3
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	11
Sous-total personnels permanents en activité	**17**
Enseignants-chercheurs et chercheurs non permanents et assimilés	4
Personnels d'appui non permanents	4
Post-doctorants	0
Doctorants	2
Sous-total personnels non permanents en activité	**10**
Total personnels	**27**

EVALUATION

Overall assessment of the team

The research activity and scientific production of the team are excellent (publications in Chest, Environment international, Science of the Total Environment in leading position and New England Journal of Medicine in collaboration). The attractiveness of the team is outstanding as attested by the high level of external funding over the assessment period (4360 k€) and recruitment of three researchers and one ingeener. The visibility of one member of the team is`outstanding (director of Fondation Alzheimer and Chair of the European Joint Program on Neurodegenerative Disease Research) and invitations to national and international conferences (Alzheimer Association International Conference Human Brain Summit). The societal impact is excellent: management of morbidity registries in the field of stroke and cardiovascular diseases, which will be matched to medico-administrative datas (SNDS).

Strengths and possibilities linked to the context

The team published a total of 177 articles, including 31 in leading position in specialised journals (Chest, Nephrol Dial Transplant, Environemental Research, European Journal of Neurology). 70 articles (representing 39% of the total), are signed as a collaborator and are the result of the team's participation in several international consortium on cardiovascular risk factors (Euroaspire, NCD-RisC Consortium, Global cardiovascular risk consortium), including one article published in the New England Journal of Medicine.
The team was successful in obtaining regional, national and international fundings. European grants one grant as PI from the European Joint program for neurodegenerative diseases and EBRA (43 k€, 2019–2024; 90 k€, 2018–2022). The team obtained one national grant from the health data hub as PI (135 k€), two grants as PI from the DGOS for the stroke registries led by the team (110 k€ each), and one grant from Santé publique France for the registries (1476 k€). As PI they also obtained one grant from the Labex (531 k€) and two grants from the Société Francophone de Néphrologie Dialyse et Transplantation (15 k€ and 10 k€).
The team recruited three researchers, one ingeener and two physicians for the morbidity registries, creating a new dynamic of research with the development of an axis related to chronic kidney diseases that share risk factors with cardiovascular diseases.
One member of the team is highly visible at the national and international level in the field of Alzheimer and other neurodegenerative diseases: head of the Fondation Alzheimer in France and chair of the European Joint Program on Neurodegenerative Disease Research. The team also has an internationally recognised expertise in the study of genetic components of the chronic diseases (particularly neurodegenerative and cardiovascular diseases), specifically in genome-wide association studies. The team participated in the organisation of the European Joint Program for Neurodegenerative Diseases, and the scientific days of the Foundation Alzheimer in France. Several members of the team participate in national instances (Inserm CSS6), and interact with local authorities (Communauté Urbaine de Lille on the topic of environmental risk factors).
The team was active in communicating with the public through different media on stroke, Alzheimer's disease and Covid-19. During the Covid-19 crisis, they developed a score to measure the risk of developing severe forms of the disease in order to inform older people with chronic diseases. This score was available through a website that received many connections. The team also shared with the public their expertise in the field of genetics by creating a comic book in French and in English (Genetics at heart).

Weaknesses and risks linked to the context

A number of staff departures during the previous contract were not replaced. The proportion of articles as the first, last or corresponding author is only 17% of the total. The current team leader, nominated at the beginning of the previous contract in 2017, will resign in 2025. The future team leader only recently joined the team. While this is an opportunity to create new dynamics around a strong research axis related to chronic kidney disease, linking it to topics already covered by the unit, a potential risk for the future team leader is to fulfil scientific objectives.
There are few PhD students (1 defence in 2023, 1 withdrawal, 2 ongoing) with respect to researchers with an HDR (6). The visibility of the team is mainly limited to the director in the field of Alzheimer and other neurodegenerative diseases.

Analysis of the team's trajectory

The team project is ambitious and relevant, and a logic continuation of the topics developed during the past contract. The research program aims to assess: 1) the influence of chronic kidney disease risk factors and kidney

aging on cardiovascular risk; 2) the influence of healthcare practices on the incidence and prognosis of aging related diseases; and 3) the impact of environmental and genetic factors on the incidence and prognosis of these diseases. The research program will exploit in-house data (registries, cohorts and surveys) enriched with medico-administrative data, spatial and environmental data. The team has adequately trained 6 members of the unit to the use of the French medico-administrative database, and has recruited a physician with expertise on data analysis to fulfil this research program.

RECOMMENDATIONS TO THE TEAM

The committee recommend that the team continue its excellent research program. To fulfil the ambitious objectives, it is important to pursue efforts to increase the recruitment of PhD students and postdoctoral fellows. Given the disease-focused research of the team, patient involvement should be further developed and emphasised. In addition to sustaining its current visibility, it is important for the team to also develop visibility on topics such as environmental risk factors and chronic kidney diseases. The committee fully endorses a gradual transition for the future team leader to facilitate the achievement of his scientific objectives.

Team 2: Molecular determinants of cardiac remodelling and heart failure

Name of the supervisor: Ms Florence Pinet

THEMES OF THE TEAM

The team's research is focused on identifying molecular determinants of cardiovascular diseases using differential -omics approaches applied in several clinical studies, and then deciphering the pathophysiological mechanisms associated with these new determinants in various animal and cell models.
The team has technical expertise in proteomic analysis and the use of cardiomyocyte cell models, and scientific expertise in mitochondrial metabolism, autophagy and extracellular vesicles. Its clinical focus is to develop a translational research program on heart failure and cardiac remodelling.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Previous recommendations pointed out the mismatch between the number of researchers, particularly permanent ones, and the ambition of the scientific program. The scientific program remains ambitious and the team has not succeeded in recruiting new permanent researchers. The team's strategy has been to merge with Team 6, thereby reaching two permanent researchers. This strategy needs to be monitored in terms of its impact on the team's scientific program and production. The team's attractiveness has been maintained as recommended through national and international public funding.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	4
Sous-total personnels permanents en activité	**7**
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	**8**

EVALUATION

Overall assessment of the team

The scientific production of the team is very good to excellent, with publications in leading positions in Cell Death and Diseases and Circ. Heart Failure. The latter publication is also a good example of the strong implication of the team in translational research. Attractiveness is excellent, as attested by the level of funding obtained (PHC Amadeus et 1 ANR Covid-Heart) during the period and active participation in a European Cost network.

The societal impact is excellent: generation and use of Rev1 and 2 clinical cohorts and a collaborative patent.

Strengths and possibilities linked to the context

The team's scientific program is based on close collaboration between clinician researchers and basic researchers, resulting in strong translational research: 44 original publications (22 as first or last author in journals such as Cell Death and Diseases and Circ Heart Failure), and 84 clinical publications (Journal of the American Heart Association, for example). Key findings include the identification of novel biomarkers such as LIPCAR or Clusterin as prognostic indicators of cardiovascular events.
The team secured European funding (ERA4HEALTH 2024–2026, as a partner, 125k€) and national grants (1 ANR as PI, 35k€, 2021–2022) and participation to 1RHU (500k€) and several foundations (Fondation de France and 2 xFédération Française de Cardiologie, with amounts ranging from 30k€ to 110k€).
Five PhD students were trained and the team is part of a European Cost network.
The societal impact is excellent, attested by the generation and use of Rev1 and 2 clinical cohorts and a collaborative patent.

Weaknesses and risks linked to the context

The shortage of permanent researchers, with the prospect of a retirement not being replaced, weakens the team's scientific program. Absence of clinical cohorts or a preclinical model related to heart failure and ¨preserved ejection fraction' and its link to metabolic risk and aging.

Analysis of the team's trajectory

The team's trajectory remains to be clarified. The merger of teams 2 and 6 requires agreement on a scientific trajectory. The decision to focus the research program on non-genetic determinants, in particular epigenetic, epitranscriptomic and post-translational modifications, will require a review of technical and scientific skills, particularly in the field of bioinformatics for data analysis. This orientation will require confirmation of the scientific basis for the merger of teams 2 and 6, to avoid destabilising the program as a whole. However, the future scientific program is well constructed, with funding prospects, and consistent with the themes and skills of the merged teams. The prospect of studying inhibition of post-translational modification of O-GlcNAcylation in heart failure is an interesting one, as it is related to the future units' other areas of expertise.
The move to a new building will require ensuring that the research program is in line with local technical facilities and does not destabilise the team.

RECOMMENDATIONS TO THE TEAM

The committee recommends preserving the link between cardiologists and researchers in the future project in order to continue developing high-level translational research.

Team 3: Molecular determinants of Alzheimer's disease and related disorders

Name of the supervisor: Mr Jean-Charles Lambert

THEMES OF THE TEAM

Team 3 focuses on the genetics of Alzheimer's disease (AD), linking disease susceptibility to pathophysiological features of the disease such as synaptic loss or metabolic modifications of molecular players (phosphorylation of tau protein or amyloid metabolism). In recent years, the team has made significant breakthroughs by leading major consortia such as the EADB (European Alzheimer & Dementia Biobank) and ADES (Alzheimer Disease European Sequencing), both of which have contributed to the identification of new genetic loci associated with AD. The team is positioned as a leader in the field of AD genetics, with the aim of transferring these genetic discoveries to preclinical biological models such as induced pluripotent stem cells (iPSCs) and Drosophila.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Team 3 has made considerable progress in implementing the recommendations of the previous report. It maintained its leading role in the field of AD genomics, as shown by its participation in major international consortia. It has also raised its international profile, notably through major publications and collaborations. The team has succeeded in promoting young scientists, and the objective of increasing the number of researchers with HDR has been reached. Recruitment has been very active, with the addition of new postdocs and permanent researchers. However, the biostatistics workforce still requires strengthening. Team 3 has continued to secure substantial funding. Collaborations with industry and opportunities for exploiting intellectual property still need to be further developed.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

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	3
Personnels d'appui à la recherche	6
Sous-total personnels permanents en activité	**13**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	3
Post-doctorants	7
Doctorants	7
Sous-total personnels non permanents en activité	**18**
Total personnels	**31**

EVALUATION

Overall assessment of the team

The team's scientific production is outstanding (2 Nat. Genetics in leading position). Its attractiveness is excellent to outstanding: partner of the EU Joint Programme – Neurodegenerative Disease Research (*JPND*, 2.3 M€), recruitment of international young scientists and PhD students (Argentina, Brazil, Italy, India, and Spain). Members of the team obtained national awards (Claude Pompidou and Joel Menard prizes).
The societal impact is very good to excellent: communication in social media and participation in public events. Overall, Team3 is a driving force in the field, with strong potential to continue making impactful discoveries in Alzheimer's research.

Strengths and possibilities linked to the context

Team 3 is very well organised, both quantitatively and qualitatively: seven permanent researchers, six ITA with permanent positions, seven postdocs and eight PhD students. This ensures a dynamic and collaborative environment, enabling the team to effectively pursue ambitious, multidisciplinary research projects.
The team has been particularly successful in securing competitive funding at national and international levels. It has led two major consortia - the European Alzheimer & Dementia Biobank (EADB) and the Alzheimer Disease European Sequencing (Ades) - which have significantly advanced genetic understanding of AD. These projects, supported by substantial grants, (La bex Distalz 888k€, JPND 2.3M€), have placed Team 3 at the forefront of AD research at the international level. The team also obtained funding (Labex, CPER...) for the acquisition of important equipment and state-of-the-art technological platforms (spinning disk, multi-electrode arrays, Nadia microfluidic system for single-cell transcriptome).
The team published 60 original articles, including several landmark papers in leading position that are among the most cited in the field and published in prestigious journals such as Nature Genetics, Neurology and Acta Neuropathologica. Their work on the genetics of AD, including the identification of new risk loci and the exploration of biological models, is widely recognised internationally. Team members participate to national evaluation processes ("La Caixa" ANR), international thesis committees, and international conferences (Alzheimer's Association International Conference). The team attracted and trained young researchers, some of them international (Argentina, Brazil, Italy, India, and Spain). Team members obtained the Prix Claude Pompidou and Prix Joel Menard. Team 3 regularly communicates on social networks (especially X and LinkedIn), and participates in public events such as 'Entretiens Alzheimer' organised by the Alzheimer's Research Foundation or '5 à 7' conference on Alzheimer's day. Team members contributed to the development of open science by making their data and research results available to the public.

Weaknesses and risks linked to the context

Although Team3 has made considerable progress in the field of AD genetics, there are still areas for some improvement. One of the main challenges is the absence of a dedicated biostatistician, which has been noted as a shortcoming in taking full advantage of the team's extensive genome-wide studies.
Maintaining funding levels beyond 2026, particularly after the end of Labex Distalz funding, poses a potential risk to the continuity of their ambitious projects.

Analysis of the team's trajectory

The project of team 3 is a natural and well-designed continuation of its work deciphering the genetic landscape of AD. The team's focus on synaptic dysfunction as a central aspect of AD pathology is innovative and highly relevant, particularly with the emphasis on genetically driven synaptic failures that could lead to tau hyperphosphorylation and subsequent disease progression. The integration of cutting-edge methodologies, such as CRISPR-Cas9, microfluidic devices and high-content screening, ensures that the team is well placed to make significant advances in the post-genomic era. The overall project is ambitious and supported by substantial funding, including major contributions from academic sponsors and foundations. The development of new models (IPSC, organoids, etc.) is well planned to understand AD at the molecular and cellular levels. The inclusion of large-scale proteomic analyses is important and will further strengthen the team's research potential. The trajectory is well integrated into broader research efforts, such as the Mosaic program, enabling collaborative synergies and interdisciplinary approaches. The project is also well aligned with Team 3 expertise, building on its previous successes while extending to new frontiers, including the study of rare genetic variants and their impact on the progression of AD. Overall, the team's trajectory is credible and innovative, with a solid foundation for continued success.

RECOMMENDATIONS TO THE TEAM

The committee recommends that Team 3 continues its outstanding research into the genetics of AD and its innovative projects focusing on synaptic dysfunction and risk factors for AD. Although the team has succeeded in securing significant funding and establishing itself as a leader in the field of AD genetics, further efforts could be made to improve translational research through further integration of clinicians within the team (to take into account the presence of co-pathologies in its research) and the establishment of industrial partnerships and file patent applications. The selection of genes for future experimental development (IPSC, etc.) should be carefully considered. The recruitment of a specialised biostatistician would allow the team to fully exploit the genetic data it generates.

Team 4: Integrative structural biology

Name of the supervisor: Ms Isabelle Landrieu

THEMES OF THE TEAM

The project of team 4 focuses on understanding how various post-translational modifications (PTMs) influence Tau (dys) functions in Alzheimer's disease (AD), while also exploring and identifying new compounds with therapeutic potential. In addition to AD, the team also studies a range of topics, including amyloid formation, transcriptional regulation, cell signalling, and host-pathogen interactions. Additional research areas include transcriptional regulation by the Mediator complex, the study of intrinsically disordered proteins (IDPs) with poly-proline regions linked to neurodegenerative diseases, and the Mpro protein of Sars-CoV-2. To achieve their goals, team 4 employs an integrated structural biology approach, utilising multiple techniques, with NMR being one of the key methods.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has made efforts to integrate cellular aspects into structural studies, as demonstrated by two publications over the last five years (Sartori et al.. Acta Neuropathol. 2019 in collaboration with Team 3, and Denis et al. Mol Therapy 2022 in collaboration with U1172 Lille Neuroscience and Cognition). Additionally, a PhD student co-supervised by a researcher from Team 3 helped bridge the gap between structural biology and cellular aspects, extending the work to Drosophila models. The strong team cohesion noted in the previous report has been maintained following the transition period, although there is mention of insufficient mentoring for young scientists joining the group. In terms of infrastructure recommendations, the team has received support from the CNRS Biology Institute to continue utilising the scientific equipment located in Villeneuve d'Ascq. Additionally, Team 4 was encouraged to develop emerging research topics at the interface with other teams in the unit. However, this effort has primarily been limited to a collaborative project with Team 6, with little significant progress in other research areas.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	4
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	6
Sous-total personnels permanents en activité	**16**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	3
Post-doctorants	2
Doctorants	3
Sous-total personnels non permanents en activité	**8**
Total personnels	**24**

EVALUATION

Overall assessment of the team

The scientific production of the team is excellent with publications in specialised journal with highest rank in the field (Angewandte Chemie 2020 and 2021, Molecular Therapy 2022). The team's attractiveness is excellent to outstanding, with high success in grant funding (Distalz Labex as partner, 12 ANR-backed projects and 2 as PI, 3ANRS, for a total of 5 M€), and international recognition as evidenced by invitations to international conferences (e.g. EURO-ISMAR, EuroTau, SMASH), and by the coordination of TAME, the first Tau European network. The team hosted several international PhD students and postdocs. The interaction with the non-academic sector is excellent for a team focused on fundamental research, with notably one patent on the therapeutic use of nanobodies targeting the tau protein.

Strengths and possibilities linked to the context

Team 4 demonstrates significant strengths and potential in its scientific expertise and its multidisciplinary approach. Located at the CNRS campus, the team consists of nine senior researchers and six highly qualified engineers, specialising in protein biochemistry, X-ray crystallography, NMR spectroscopy, and cryo-EM.
The team has gained international recognition for its impactful research on amyloid diseases, nanobodies, and innovative NMR methods, contributing to global understanding of neurodegenerative diseases, particularly Alzheimer's. Team 4 coordinates the first Tau Network Of Europe (TAME), a consortium of 9 European laboratories. Team 4 members were invited to speak at prestigious conferences, such as EURO-ISMAR in Berlin in 2019, the XIIth international conference NMR a tool for Biology in Paris in 2021, and the FGMR-GDCh meeting in Karlsruhe in 2022. They hold key roles in scientific associations including president of the national Germ association, and serve on national research committees such as Hcéres and CoNRS. Their contributions have been further recognised through individual awards, such as the 'Médaille de Cristal Collectif du CNRS' and CNRS Excellence in Research awards.
The team fosters a supportive environment for young scientists, encouraging PhD students and postdocs to lead publications and participate in international conferences.
A key strength of Team 4 lies in its ability to secure substantial funding, raising 5 M€ from various sources, including twelve ANR grants (10 as partners and 2 as coordinator) and prestigious international partnerships, such as collaborations with Alzheimer's research teams under the PIA Distalz Labex program. This financial support has allowed for essential equipment investments, such as NMR spectrometers equipment, and has facilitated the retention of young talent. The team's involvement in European projects, such as the ITN TASPPI and EU MSCA Doctoral Network Tame TauImmune, as well as partnerships with laboratories in Germany and Portugal, highlights their strong international presence and collaborative network.
Team 4 operates state-of-the-art NMR facilities, including a 900 MHz spectrometer integrated into the national Infranalytics infrastructure, and have initiated numerous collaborative projects, particularly through specialised equipment such as the 600 MHz cryo-probe for Fluorine detection. Significant investments have been made in infrastructure, including helium recycling and new equipment for protein preparation and cryomicroscopy. Team 4 published 65 peer-reviewed publications, with some of them in high-impact journals, for example Molecular Therapy and Angewandte Chemie as last authors. Their work on Tau protein aggregation and the development of therapeutic nanobodies resulted in a patent in 2019. This project gained further recognition with support for bioincubation from the regional incubator Eurasanté in June 2020 and by a grant from the Alzheimer association/Rain Water Foundation (240 k€), underscoring the promising potential of this therapeutic approach. The team also has numerous interactions with companies through collaborative research projects (notably with Astra Zeneca, Taros chemicals and Hybrigenics services, and by providing NMR services.

Weaknesses and risks linked to the context

The team had limited success in securing doctoral fellowships funded by the university (3 PhDs for 7 HDR).
The absence of a first-line cryo-electron microscope limits their research capabilities in this field, and their efforts to advocate for better local infrastructure are challenged by the small number of researchers in their field on campus, making it difficult to achieve the necessary critical mass for institutional support.

Analysis of the team's trajectory

The team is transitioning towards a new UMR CNRS-ULille structure, with the existing EMR 9002 serving as the foundation for this new unit. While the administrative relationship with the Lille Pasteur Institute will change, the team intends to maintain collaborations established within the Institut over the past years.

The team will continue strengthening its biophysical expertise, particularly in structural and molecular biology, employing advanced techniques such as X-ray crystallography, NMR spectroscopy, and cryo-EM.
Key priorities for the future include supporting the career progression of a young scientist within the team, specifically helping them apply for a CNRS position and an ERC Starting Grant. The team is also committed to expanding its expertise in Cryo-EM and hopes to secure a state-of-the-art 100 keV microscope to further this goal. Collaboration with physiology and medical experts will be a central theme moving forward, as will continued involvement in open science initiatives.
The team will continue to focus on understanding protein-protein interactions, with an emphasis on IDPs, particularly the Tau protein, which is central to neurodegenerative diseases like Alzheimer's. The team is also pursuing the preclinical development of tau nanobodies through a new startup initiative, signalling a significant step toward translating their research into real-world clinical applications. Moreover, the team is preparing to adapt its research priorities in response to the evolving French national research strategy, particularly under the PEPR (Programme et Équipements Prioritaires de Recherche).
The team seeks to develop ultrahigh-resolution NMR techniques applicable to intrinsically disordered proteins (IDPs), utilising Fluorine-19 NMR to explore the relationship between repeated sequences and the aggregation tendencies of disordered proteins implicated in neurodegenerative diseases. Additionally, the team plans to investigate Mediator complex interactions with transcription factors in cancer, while also further characterising the assembly and dynamics of viral proteins associated with diseases such as Hepatitis C and coronaviruses.
In summary, the team is evolving both structurally and scientifically, aiming to enhance its research capabilities while addressing pressing biological questions, particularly in neurodegenerative diseases and viral pathogenesis. The team faces difficulty in recruiting qualified and motivated young researchers. In parallel, two U. Lille faculty members (one MCU and one professor), will leave the team, and one DR2 researcher will retire by January 2025. This will result in the loss of three permanent positions, creating uncertainty about the team's long-term staffing needs. Another concern is the high cost of maintaining essential equipment, such as the 900 MHz spectrometer, which may be excluded from the Infranalytics network in the future. The upcoming end of Labex funding further complicates their financial outlook, and the team needs to find new sources of support.

RECOMMENDATIONS TO THE TEAM

The committee recommends that team 4 continues its remarkable research into the role of Tau in AD and the Tau-Targeted nanobodies development in therapeutic and potential clinical use, and its involvement in pluridisciplinary approaches. To sustain this progress, the team must secure alternative funding as Labex support ends, diversifying their financial sources through national and international grants. The team should continue its efforts to advocate for better local infrastructure, especially in cryo-electron microscopy, which could significantly enhance their research capacity. The team is encouraged to refine its scientific focus to achieve greater coherence between the different projects.

Team 5: Glycation: from inflammation to aging

Name of the supervisor: Eric Boulanger

THEMES OF THE TEAM

Team 5 studies the fundamental mechanisms of aging and resilience without focusing on a single organ or disease, but considering a geroscience approach through the involvement of advanced glycation products (Ages) and the RAge axis (receptor for Ages) in recovery after an acute inflammatory shock (inflammaging). The team carries out a multidisciplinary and translational research, from the search for biomarkers of aging to the development of a drug candidate. The team aims to transfer geriatric expertise to society using digital tools to detect and prevent pathological aging.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Team 5 responded to all of the previous recommendations by welcoming 6 postdoctoral fellows in order to broaden its scientific program towards non-permanent researchers and doctoral students, by restoring gender balance within the team, and by developing its translational research program, notably through organoids and the program of drug discovery.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

Catégories de personnel	Effectifs
Professeurs et assimilés	8
Maîtres de conférences et assimilés	6
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	**16**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	4
Post-doctorants	3
Doctorants	5
Sous-total personnels non permanents en activité	**13**
Total personnels	**29**

EVALUATION

Overall assessment of the team

The scientific production of the team is very good to excellent, with publications in highly ranked specialised journals in their field (Kidney Int, Aging Cell) in leading position. The team's attractiveness is excellent: European funding (as partner, Interreg and EJPRD) and national competitive funding (2 ANRs as PI), CPER and Startairr, for a total of 1.7 M€. The team's high visibility is further shown by team members serving on the board of the European Geriatric Medicine Society, the organisation of international meetings ('Biology of Aging' session of the European Geriatric Medicine Society), and participation to international conferences. Eighteen PhD students were hosted and fifteen defended.
Societal impact of the team is overall excellent with three patents in collaboration with Junia and transfer knowledge on aging to society through the Tempoform application for detecting and preventing pathological aging (31,500 connections to date).

Strengths and possibilities linked to the context

Team 5 includes multidisciplinary researchers developing studies on molecular mechanisms involving Ages and translational research. The team has extensive technical expertise in physiology, Ages chemistry, mitochondrial metabolism, cell biology, organoid models, and other animal models of aging. The translational approach and, in particular, the prospect of developing new biomarkers of aging and new drugs, endow it with a high potential for scientific and commercial development. The team has developed a strong support program for doctoral and post-doctoral students, making it highly attractive both nationally and internationally (18 PhDs during the contract were hosted, 14 theses defended for 15 HDR).
The team published 64 articles including 45 in leading position. Among these, some are published in top journals of their discipline (Kidney international, Aging cell, Chem eur J). Of note, they demonstrated that invalidation of the receptor for Age delays physiological and Carboxymethyllysine-accelerated aging in mice (Aging Cell 2018). Their experience in combinatorial chemistry has enabled them to develop new ligands of AgeR as potential antagonists of Age (Chem Eur J 2024). The team was successful in securing national competitive funding: 1.7 M€ during the contract with four international grants including one Interreg and one EJPRD as partner, one UEFISCDI as PI, and three ANR grants (2 as PI). The team's work is internationally well recognised in their domain, as attested by participation to meetings in the respective speciality (75 conferences) and organisation of the annual 'Biology of Aging' session of the European Geriatric Medicine Society (2022-23). They are on the board of international societies such as the International Maillard Reaction Society and the European Geriatric Medicine Society. They organised international meetings such as 'Advances in Pharmaceutical Analysis' and Sustainable Drug Discovery Day' with the universities of Gent (BE), Groningen (NL) and Gdańsk (PL). Members of the team are involved in national (Hcéres, Inserm CSS) and international expertise (EU Marie Skłodowska-Curie Postdoctoral Fellowships call and Eiffel programme). Several unit members are heavily involved in teaching and have university responsibilities (Vice-Dean in charge of research at the Faculty of Medicine Univ Lille, deputy member of CNU, members of the UFR3S council of the University of Lille). The team filed three patents in collaboration with JUNIA and developed an app (tempoform) tht already has 31,500 connections.

Weaknesses and risks linked to the context

The number of publications in high-impact journals is low in relation to total publications

Analysis of the team's trajectory

The scientific program for next term is coherent and in line with the current program and the team's skills. In addition to maintaining the Ages and Rages themes, the program will focus on the exploration of senescent cells and their role in inflammaging through their interactions with Ages. The program is clearly structured, offering a natural progression between prevention, pathophysiology and drug discovery.
The team is developing a program on healthy aging, with the creation of a longitudinal cohort that offers numerous prospects and anchors the program in the perspective of translational research with applications in clinical practice (biomarkers and development of new drugs). The dispersion of the team over three sites, in a context of limited space, and expansion of the scientific research themes may lead to the dispersion of resources and a reduction in scientific productivity.

RECOMMENDATIONS TO THE TEAM

The committee recommends to the team to concentrate their effort to publish their work in high impact journals.

Team 6: Molecular and cellular pathophysiology of metabolic diseases

Name of the supervisor: Jean-Sébastien Annicotte

THEMES OF THE TEAM

The team 'Molecular and Cellular physiopathology of metabolic diseases' studies novel environmental factors involved in the onset, development and evolution of cardiometabolic diseases, using integrated functional approaches in cellular and mouse models. Specifically, the team worked on the link between reduced beta-cell mass and insulin secretion defects during the course of type 2 diabetes (T2D), and the role of pluripotent stem cells in peripheral adipose tissue insulin resistance.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

In spite of major events that had a direct impact on its research activities, including its move from UMR1283 to UMR117 Ridage (validated by Inserm CSS3 and ITMO PMN), the team was able to follow previous recommendations and maintain high-quality papers in the 2018–2023 period and increase its publications (from 10 to 24). There was no specific recommendation for the team's organisation, but it should be noted that after joining UMR1167, the team was able to adapt to the new environment and developed strong collaboration with team 2 that led to a merge for the next mandate with a common trajectory. Regarding the scientific strategy and projects, the move of the team from UMR1283 did not allow stronger interaction with their former colleagues, but translational research from murine beta cells to human beta cells is currently being developed.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2023

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	0
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	**2**
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	1
Sous-total personnels non permanents en activité	**3**
Total personnels	**5**

EVALUATION

Overall assessment of the team

The teams' scientific production is very good to excellent (considering its relocation midway through the assessment period and the loss of one third of its staff), with publications in leading position in excellent journals including Cell Rep and Diabetes. The attractiveness is also excellent for the size of the team: funding for a total of 2 M€, including three ANR-backed projects (2 as leader), one prestigious FRM labelling, invitations to international (European Group for the study of insulin resistance), and national (SFD, SFE) conferences, participation of team members to scientific evaluations (vice president ANR committee).
The interaction with the non-academic sector is also excellent: one industrial chair, three maturation grants from SATT Nord, and yearly outreach activities (general audience in different media).

Strengths and possibilities linked to the context

The team was highly succesfull in securing funding: European Foundation for the Study of Diabetes as PI, three ANRs (two as PI: Betapasticity (591k€) and epiRNAT2D (694k€), one as partner MetaboTAU (720k€)), one FRM team label as PI (350k€), one regional CPRE 'longévité as PI and several PhD contracts or grants for valorisation, for a total of 2000k€. In spite of the presence of only one senior researcher for half the mandate (2022–2024, following relocalisation to Ridage), the team published 24 manuscripts (11 articles in leading positions in top-notch journals such as Mol Metab, Biomolecules, Cell Rep, Diabetes and iScience, and co-authored articles in JCI, Nat Cardio Res, Nat Comm, Nat Metabo, etc..). PhD students co-authored several team papers: first author in Cells 2022, 2023, Cell Rep 2022, Biomolecules 2020, co-authors in Diabetes 2023 and other journals. One PhD student secured her own funding (Isite ULNE AAP). Post-docs authored articles in Diabetes 2023, iScience 2023, Cells 2022, 2023, and Cell Rep in leading position. The team developed internal collaboration with other Ridage teams (e.g. team 2) as illustrated by joint publications (Biomed 2022; JCI 2022). The team leader was invited to several national and international conferences (EUGSIR, EMBO workshop, SFD, SFE), organised scientific events (IPL longeviry seminar, SFD-Langerhans) and participated in several steering committees (EuC FET-Open, EIC pathfinder, MRC UK, Hcéres expert, ANSES and ANR as vice-president CE14). All young scientists participated to conferences (EURGSIR; SFD, École thématique EGID, etc.). Two promotions took place (1CRCN to DR2 Inserm and 1 TCN to AI IPL). The team leader is part of a COST network. The team obtained one industrial chair (400k€, 2020–2021 with Aptamir), one industrial contract with Ingredia (25k€) and obtained two additional maturation grants from SATT Nord (SATT Nord 293k€ and Startair 133k€). Members of the team actively participated to UMS PLBS platforms (by obtaining funding for equipment such as Pamgene kinome profiling, Seahorse metabolic flux, insulin secretion platform). The team communicated widely with the general audience in different media: invitations to TV news (France 3) as well as the web press campaign, and participation in 'Fête de la Science'.

Weaknesses and risks linked to the context

No major weakness.
Integration and fusion of two teams are a high-risk high-gain strategy and requires attracting more local and foreign students to eventually postulate for permanent positions (Inserm, CNRS, University), and reinforce the recruitment of new permanent researchers.

Analysis of the team's trajectory

For the next term, the team will merge with team 2, whose leader is retiring, providing a new but complementary research trajectory (validated by Inserm CSS3 and ITMO in 2024). The team will be named 'Molecular and cellular pathophysiology of cardiometabolic diseases' (CardioDab) and move to the Institut Pasteur de Lille campus in June 2024. The team will decipher how environmental factors shape epigenetic, epitranscriptomic and post-translational modifications to translate into an adaptive cellular response influencing gene transcription, protein translation and function, and contributing to the maintenance of metabolic homoeostasis. This project reflects the complementarity of the teams' themes (cardio and metabolism), and is a perfect match with the PI's expertise and the unit's objectives. Understanding cellular plasticity and organ cross-talk dysfunctions could lead to novel therapeutic perspectives for cardiometabolic diseases such as heart failure, obesity and type 2 diabetes. Three main research axes will be developed 1) study of the epigenome and epitranscriptome signatures in T2D/heart failure (murine transgenic models and REVE1/2 human cohorts); 2) study of the inhibition of post-translational modification O-GlcNAcylation in acute decompensated HF (repurposing of Thiamet G in a

rat model of acute decompensated HF and validation in hu cardiac biopsies), and search of new biomarkers and 3) development of a multi-organ *in vitro* model (use of hiPSC-cardiomyocytes to study cardiac function and development of iPSC for other differentiation states +/- microfluidics).

RECOMMENDATIONS TO THE TEAM

The restructuring (merge of TEAM2 and 6 from UMR1167-Ridage validated by Inserm CSS3 and ITMO PMN) has what it takes to pursue a remarkable and innovative research program. The recruitment of one CR would be an additional force to ensure success. Better integration of all team members into the life and strategy of the team should be considered. Together with the strong ability of the team leader to raise funding, and a new administration, this would provide the opportunity to further invest time and efforts into European Grant applications. Special attention should be paid to maintain a good balance between the many collaborations, the new research themes of the team, and responsibilities of individual lab members, in order to avoid dispersion. The merge of the team with two PU-PHs provides a unique opportunity to reinforce clinical papers or translational studies.

CONDUCT OF THE INTERVIEWS

Dates

Start: 22 October 2024 at 9 a.m.

End: 23 October 2024 at 5 p.m.

Interview conducted: on-site

INTERVIEW SCHEDULE

Day 1 Amphithéatre Buttiaux, Bâtiment Calmette

1:15 p.m.-2 p.m. closed-door meeting of committee

2 p.m.-2:10 p.m. presentation of the committee

2:10 p.m.-2:50 p.m. Philippe Amouyel and Jean-Charles Lambert, Unit presentation, open to all
(20 minutes presentation, 20 minutes questions)

team presentations (35 min each)
(15 min presentation, 15 min questions; 5 min PI alone with the committee for PIs renewing contract)

2:50 p.m.-3:25 p.m. Team 1 Aline Meirhaeghe and Aghiles Hamroun
3:25 p.m.-3:45 p.m. Team 2 Florence Pinet (bilan)
3:45 p.m.-4:20 p.m. Team 6 Jean-Sébastien Annicotte
4:20 p.m.-4:50 p.m. Coffee break, committee deliberation

4:50 p.m.-5:25 p.m. Team 3 Jean-Charles Lambert
5:25 p.m.-6 p.m. Team 4 Isabelle Landrieu

6 p.m.-6:35 p.m. Team 5 Eric Boulanger
6:35 p.m.-7:15 p.m. committee debrief of the day

Day 2, October 23, Amphithéatre Buttiaux, Bâtiment Calmette

8:30 a.m.-9 a.m. arrival of committee/coffee
9 a.m.-9:30 a.m. Discussion with PhD students and postdocs (closed doors)
9:30 a.m.-10 a.m. Discussion with research scientists (closed doors)
10 a.m.-10:30 a.m. Discussion with technical and administrative personnel (closed doors)

10:30 a.m.-11 a.m. debriefing of committee

11 a.m.-11:30 a.m. Meeting with the managing bodies
Frédéric GOTTRAND, CHU de Lille
Olivier COLOT, Université de Lille
Fabienne JEAN, Frederic BATTEUX, Institut Pasteur Lille
Hugues LORTAT-JACOB, INSB CNRS
Robert BAROUKI et Arnaud DE GUERRA IT Inserm
Chantal BOULANGER, Raymond BAZIN IT PMN Inserm

11:30 a.m.-11:45 a.m. Meeting with secondary managing bodies:
Benoit ROBYNS, VP Recherche JUNIA
Dominique LACROIX, Dean UFR3S

11:45 a.m.-12:15 p.m. Closed-door meeting of the committee (in presence of the Hcéres scientific advisor)

12:15 p.m.-12:45 p.m. Discussion with the directors

12:30 p.m.-4:05 p.m. Final debriefing with lunch - Finalising of the report

PARTICULAR POINT TO BE MENTIONED

NA

GENERAL OBSERVATIONS OF THE SUPERVISORS

RÉPUBLIQUE FRANÇAISE
Liberté Égalité Fraternité

Université de Lille

—

Direction générale déléguée
Recherche et valorisation

Les vice-présidents recherche de l'Université de Lille

à

HCERES - Département d'Evaluation de la Recherche

Lille, 24/02/2025

Objet : Courrier d'observation de portée générale Université Lille DER-PUR260024873

Direction générale déléguée
Recherche et valorisation
Direction d'Appui à la Recherche

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Chère, Cher collègue

L'université de Lille tient tout d'abord à remercier le comité de visite HCERES pour l'attention qu'il a portée au travail mené par l'unité RID-AGE – Facteurs de risques et déterminants moléculaires des maladies liées au vieillissement - et pour la qualité de l'évaluation qu'il a produite.

Le comité de visite a été l'occasion, pour les membres de l'Unité de Recherche et pour l'Université, d'approfondir certaines questions et de répondre aux interrogations des experts, dans un esprit constructif dont il faut se féliciter.

Les recommandations émises dans le rapport d'évaluation seront précieuses pour l'unité pour le déploiement de son projet lors du prochain contrat.

Vous trouverez ci-joint un relevé des erreurs factuelles à corriger en vue du rapport définitif.

Nous vous prions de croire, chère collègue, cher collègue, à l'expression de notre considération distinguée.

Pour le Président et par délégation,
Les Vice-Présidents Recherche de l'Université de Lille

Olivier Colot Sandrine Chassagnard

—
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