Research evaluation

# EVALUATION REPORT OF THE UNIT

C2VN - Centre de recherche en cardiovasculaire et nutrition de Marseille

## UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

INRAE
INSERM
Aix-Marseille Université

**EVALUATION CAMPAIGN 2022-2023**
GROUP C

Report published on July, 11 2023

In the name of the expert committee[1] :

Ingrid Fleming, Chairwoman of the committee

For the Hcéres[2] :

Thierry Coulhon, President

Under the decree n° 2021-1536 of 29th November 2021:
[1] The evaluation reports "are signed by the chairperson of the expert committee". (Article 11, paragraph 2);
[2] The president of the Hcéres "countersigns the evaluation reports established by the expert committee and signed by their chairperson." (Article 8, paragraph 5).

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

## MEMBERS OF THE EXPERT COMMITTEE

| | |
|---|---|
| **Chairperson:** | Mrs. Ingrid Fleming, Goethe University Frankfurt, Germany |
| **Experts:** | Mrs. Pascale Gaussem, Université de Paris Cité<br>Mr. Xavier Collet, Inserm, Toulouse<br>Mrs. Stéphanie Venteo, Inserm, Montpellier<br>Mr. Benoit Guillet, Rennes (CNU)<br>Mr. Philippe Gerard, INRAe, Jouy-en-Josas |

## HCÉRES REPRESENTATIVE

Mrs. Florence PINET

# CHARACTERISATION OF THE UNIT

- Name: CardioVascular and Nutrition research Center
- Acronym: C2VN
- Label and number: UMR Inserm 1263, Inrae 1260
- Number of teams: 5
- Composition of the executive team: ALESSI Marie-Christine

## SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement

SVE6: Human Physiology and Physiopathology, Ageing

SVE7: Prevention, Diagnosis and Treatment of Human Diseases

## THEMES OF THE UNIT

The themes of the Center for CardioVascular and Nutrition Research (C2VN) focus on nutrition, vascular biology, thrombosis and haemostasis. The unit is currently structured around five teams that are committed to combining basic research with translational programs to better understand, prevent, diagnose and/or treat vascular, heart, metabolic, kidney and/or respiratory diseases. The unit achieves this by working on haemostasis, thrombosis, endothelial homoeostasis, heart adaptation and the exposome as core mechanisms.

## HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The founder teams of C2VN were the NORT Unit (Nutrition, Obesity and Thrombosis – INSERM 1062/INRAE 1260 under the directorship of Mrs Marie-Christine Alessi) located at the Timone university hospital campus at the Faculty of Medicine and the VRCM Unit (Vascular Research Center of Marseille – INSERM 1076 under the directorship of Mrs Françoise Dignat-George) is located at the Faculty of Pharmacy. They were joined by the MD2 Unit (Dysoxia–Hyperactivity: cellular and integrated therapies) at Aix-Marseille University under the directorship of Mr Régis Guieu located at the North Campus. C2VN consists of five teams, with Mrs MC Alessi as Director and Mrs F. Dignat-George as deputy director.
Teams 1 and 2 are located at the Faculty of Medical and ParaMedical Sciences (MPMS), while teams 3, 4, 5 are located at the Faculty of Pharmacy. MS-Nutrition, a start-up created by the NORT unit, is housed at the Faculty of MPMS. Remedex, a start-up created by team 3, is located on private premises.

## RESEARCH ENVIRONMENT OF THE UNIT

C2VN was created by INSERM, INRAE and Aix-Marseille University (AMU), and the unit has benefited from the fact that the five teams are all housed at the same campus. A major goal for the next contract is to gather the teams under one roof at the faculty of Pharmacy. C2VN has greatly benefited from the support of the A*midex, RHU4, RHU PIONeeR, GENMED LabEx, and is a member of the 'Equipex+ HIPE' project.

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

| **Permanent personnel in active employment** | |
|---|---|
| Professors and associate professors | 41 |
| Lecturer and associate lecturer | 33 |
| Senior scientist (Directeur de recherche, DR) and associate | 8 |
| Scientist (Chargé de recherche, CR) and associate | 12 |
| Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées) | 7 |
| Research supporting personnel (PAR) | 48 |

| | |
|---|---|
| **Subtotal permanent personnel in active employment** | **148** |
| Non-permanent teacher researchers, researchers and associates | 1 |
| Non-permanent research supporting personnel (PAR) | 36 |
| Post-docs | 11 |
| PhD Students | 63 |
| **Subtotal non-permanent personnel** | 111 |
| **Total** | **259** |

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

| Employer | EC | C | PAR |
|---|---|---|---|
| Aix-Marseille Université | 61 | 16 | 28 |
| Inrae | 0 | 5 | 6 |
| Inserm | 0 | 13 | 12 |
| Cnrs | 0 | 3 | 0 |
| Ministère des Armées | 0 | 1 | 0 |
| Université de Toulon | 0 | 1 | 0 |
| CHU Marseille | 0 | 0 | 2 |
| **Total** | **61** | **39** | **48** |

## UNIT BUDGET

| | |
|---|---|
| Recurrent budget excluding wage bill allocated by parent institutions (total over 6 years) | **3,297** |
| Own resources obtained from regional calls for projects (total over 6 years of sums obtained from AAP idex, i-site, CPER, territorial authorities, etc.) | 386 |
| Own resources obtained from national calls for projects (total over 6 years of sums obtained on AAP ONR, PIA, ANR, FRM, INCa, etc.) | 11,963 |
| Own resources obtained from international call for projects (total over 6 years of sums obtained) | 1808 |
| Own resources issued from the valorisation, transfer and industrial collaboration (total over 6 years of sums obtained through contracts, patents, service activities, services, etc.). | 6,736 |
| **Total in Keuros** | **24,190** |

# GLOBAL ASSESSMENT

C2VN is the only research centre at AMU focused on nutritional and cardiovascular disorders and was created by INSERM, INRAE and Aix-Marseille University (AMU) during the last mandate. The unit has an international visibility in the fields of haemostasis, thrombosis, vascular biology, biomarkers and micronutrients. The translational commitment of the unit is greatly aided by its proximity to healthcare facilities with a privileged connection to ten clinical departments and three clinical labs. Members of the C2VN manage hospital platforms (notably sequencing, vascular monitoring, centre for cell engineering and therapy). Also, the unit has coordinated 35 cohorts of patients as PI (platelets disorders, haemostasis MARFAST, Martha, …) and participated in 111 clinical trials and 29 PHRC (15 as PI).
C2VN has benefited from the support of the A*midex, and is a member of the 'Equipex+ HIPE' project. The recurrent dotation (Inserm, AMU, INRAE) represents 13% of the total budget while 87% comes from industry (42 industrial partnerships), PIA (RHU4, RHU PIONeeR), GENMED LabEx Europe (Training). ANR grants (n=17, 6 as PI) represent only 10% of the budget. The projects within the unit are supported by five high quality state-of-the-art technological platforms. Four of the platforms are designated AMU platforms and the fifth includes a hyperbaric platform and hypoxic chamber.
The scientific objectives of the unit are relevant as well as timely and have been modelled into excellent translational and transversal projects. The success of the program is highlighted by the fact that the research performed by teams 1, 2 and 3 is at the forefront of cardiovascular research at the national level, with each team having a strong international reputation. There is also good team cohesion with evidence of collaboration between teams documented in co-authored papers i.e. 11% (n=135) of total publications. The unit has also continued to develop since its inauguration e.g. now turning to the use of artificial intelligence, and models such as organoids. The technological developments were supported by the hiring of a bioinformatician on-site, collaborations with physicians, mathematicians, in order to study biomechanics, organ cross-talks, which are highly innovative. The unit has also managed to attract basic scientists with permanent position (n=3) to the consortium.

The publication output of the C2VN as a whole is excellent with high-level production and an improvement in comparison with the last mandate (increase of 15%). 414 original papers (34% of the total number of publications) have been published as strategic positions (first, last position, or corresponding author). In the whole, 66 (16%) are in multidisciplinary prestigious journals with large scientific readership (Nat Commun, PNAS, Nat Genet, Science Translat Med, Lancet, New Engl J. Med, JAMA Cardiol) but some other teams are used to publish in less notorious journals.
The unit has a lot of interactions with civil society on a regular basis (every year), though:

i) its participation in scientific presentations dedicated to the public,
ii) its participation in meetings with various patient associations,
iii) its activity as members of the Nutri'In Med association, which raises awareness of the relationship between health and nutrition.

The unit uses media such as

i) television programs,
ii) radio programs
iii) and mainstream journals.

Altogether, the unit shows an outstanding level of product development, notably those intended for the medical world. The work of the unit resulted in four licenses, 25 patents, and two start-ups (1 created during the last mandate).
All of these points i.e. the quality of the platforms with a translational impact for the projects, the publications and the innovations and collaborations with industry as well as the organisation of international scientific events add together to make the unit attractive and generally outstanding.

# DETAILED EVALUATION OF THE UNIT

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

The previous report was generally positive and recognised the impressive overall scientific output of the C2VN. At the time of the previous evaluation, the unit was just about to undergo restructuring/reshuffling to form five interdisciplinary teams housed in two buildings located at Timone campus of Marseille. The review panel was keen that the unit maintains the high level of their original research, their valuable collaborations nationally and internationally. The panel also made several recommendations to the Unit. These included making use of the large cohesive mass of the new unit to obtain major public grants (particularly European grants), to continue forging strong links with industry and the identification of patentable innovations, the development of effective communication across the new Unit (website or newsletter) and the optimisation of available administrative personnel. Other suggestions involved acquiring accreditation for international programs e.g. Erasmus mundi programme. With regards to research, the review panel praised the five plans but still recommended that the unit carefully consider the breadth of the future plans for all teams, and assess whether some may need to be more focused.
During the last evaluation period, many of these concerns were successfully addressed as the unit applied for a RHU (Réseau Hospital-Universitaire ») project that focused on the development of innovative vascular biomarkers with the goal of evaluating the pro-thrombotic potential of platelets and endothelium, and that played to the strengths of three of the C2VN teams. The unit also secured twelve ANR projects and two ERANET programs. The C2VN is also involved in European funded training networks and is active in the European Joint Doctorates (EJD) program. Regarding the optimisation of administrative resources and support the C2VN was able to recruit a general secretary, which seems to have had a major impact on the financial and administrative management of the unit. This reorganisation also identified internal resources that were redeployed to recruit a computer engineer who seems to be in the process of integrating C2VN data into the AMU data centre. This step is likely to improve data security and reliability as well as the generation of a mutually searchable C2VN data warehouse.
Regarding the focus of the research planned in some of the teams, the previous report panel felt that some additional focusing was warranted as was some internal critical appraisal of projects to ensure feasibility. The C2VN seems to have left this issue up to the individual teams by requesting each team to focus on the most promising topics.

## B – EVALUATION AREAS

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

#### Assessment on the unit's resources

The unit's resources are excellent, with a budget that doubled compared to that of the last mandate. The recurrent budget from institutions (AMU, Inserm, Inrae) represents 13% of the total budget with 87% coming from industries, PIA, Europe (Training).
The unit has obtained four international contracts as PI, seventeen ANR (6 as PI), 29 PHRC (15 as PI), participated in eight PIA (2 as PI) and grants from Amu (AmiDEX) and several foundations ('Fondation de France, Société Française de Diabète, Fondation pour la Recherche Médicale, Fédération Française de Cardiologie', …).
The unit is coordinators of five high quality technological platforms which four are under the umbrella of the AMU. The fifth is the hyperbaric platform and hypoxic chamber.

## Assessment on the scientific objectives of the unit

The scientific objectives of the unit have been excellently designed with a strong focus on translational and transversal projects. The research performed by teams 1, 2 and 3 is at the forefront of cardiovascular research, with each of the groups having a strong international reputation. Some of the research is highly innovative and has a 'lighthouse' character.
The unit has begun to include novel technologies (e.g. artificial intelligence as well as organoid models). They have also hired a bioinformatician, and actively collaborating with physicians and mathematicians.

The use of real-time intravital microscopy to study thrombus formation and inflammation (immune thrombosis) with top quality of images (4D camera) and extracellular vesicles study for identification of variants involved in thrombosis are unique in France.
The unit is involved in standardisation studies and international guidelines.

## Assessment on the functioning of the unit

The assessment panel judged the unit as outstanding on the basis of the success of the directors and team leaders in coordinating the different teams, developing inter-team projects (funding 2 projects per year @20 K€), as well as organising and participating in training courses (n=220 for 117 members of the unit).
The unit has benefited from a general secretary and a bioinformatician to improve the management of the lab. However it is not sufficient in terms of human resources, especially dedicated to the platforms. The management of the unit seems to be appreciated by the different members of the team (researchers, students and ITA). Many common tasks are taken over by the permanent ITAs who ask for a better distribution with ITAs in contract and students.
Over the last five years, sixteen members of the unit have been promoted. Financial bonuses for ITAs are requested and obtained each year.

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

#### Strengths and possibilities linked to the context

C2VN shares proximity with healthcare facilities with a privileged connection with ten clinical departments and three clinical labs.
The unit is organised for the recruitment of permanent research support staff and supports staff in the various promotion campaigns organised by the supervisory authorities. Over the last five years, sixteen members of the unit have been promoted (1 DR INRAE, 1 CRHC INSERM, 1 MCU HC AMU, 1 IR INSERM, 3 IGE HC AMU, 1 IGE AMU, 1 ASI AMU, TCE (1 INRAE and 2 AMU), two TCS (INSERM and AMU) and two Tech (INSERM and AMU). Six non-permanent members were recruited into a permanent position: one INRAE Tech and two IGE AMU; 1 ATRF AMU and 2 AMU Tech (CDI). The unit is consisted of 64 hospital academic researchers, nineteen pure academic researchers, and eighteen researchers (INSERM, INRAE, CNRS…)

Members of the C2VN manage hospital platforms (notably sequencing, vascular monitoring, centre for cell engineering and therapy). The C2VN has made a commitment to the integration of modern technology in its research and had made successful use of next generation sequencing, metabolomics, nanobody development, etc. The unit is coordinator of five platforms with a national visibility, four are sustained by AMU which is the BIOMET platform (biometabolomics), the real-time digital intravital microscopy platform (PIVMI) the AMUTICYT platform (cell sorting and high-sensitivity flow cytometry), and the PhenoMars platform (screens of *in vivo* and *in vitro* assays for metabolic phenotyping) and the hyperbaric platform. The unit also has access to local infrastructure. Two platforms, BIOMET and AMUTICYT, have initiated a quality approach in order to obtain ISO9001 certification.

The unit has raised substantial funds, more than 4M€/year, 85% being external grants. 22 % of funding comes from research valorisation and industrial partnership and 6% from national hospital clinical research programs (PHRCs) to support translational and clinical research. The unit devotes most of its recurrent budget (70%) to collective expenses.

The number of researchers has grown during the current contract with the recruitment of two Inserm researchers and university staff, allowing the emergence of a new team for the next mandate. The heart axis will be strengthened to focus on cardiac development in relation to metabolism and nutrition. Some members of this team already joined the C2VN in 2022.

The activities are well balanced between teams in terms of research administration dissemination, supervision, expertise, research and valorisation, around 70% activity devoted to research and its supervision.
Although some of the teams (especially teams 3 and 5) are mostly composed of clinician researchers, every team has a significant number of academic researchers and permanent technical staff from INSERM, AMU or INRAE.

### Weaknesses and risks linked to the context

The financial support for gathering all teams at the faculty of Pharmacy is lacking, making the inter-team collaborations more difficult than necessary.
The unit has insufficient perspective for the recruitment of academic researchers and foreign postdoctoral fellows.
All of the teams but two are led by two researchers, but the shared management is not precisely described.
The permanent technical and administrative staff has decreased during the current contract, with retired coworkers not being replaced, a change that will likely impair or at least delay the implementation of new techniques and assistance to researchers.
C2VN lacks qualified permanent staff such as engineers that hinders the development of bioengineering technic and bioinformatics.

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

### Strengths and possibilities linked to the context

C2VN's mission is to develop personalised cardiovascular medicine, in close liaison with APHM [the Marseille public hospital system]. C2VN has been structured into five research teams. The scientific strategy is mainly elaborated within each team.

An external scientific advisory board (SAB) met at the mid-term of the current contract.
The laboratory council meets three times a year. It is composed of the executive board members, the prevention assistants, elected staff (3 rank A, 3 rank B, 5 ITA/BIATSS representatives and three representatives of postdoctoral/doctoral students and staff members appointed by the director) to ensure proper representation of all staff.

The unit has been highly successful in many areas and on the whole generated both basic and translational data that will help better understand the molecular and cellular mechanisms involved in disease development. The focus of C2VN on combining basic research and translational programs to better understand the pathophysiology of thrombosis and vascular, cardiac, metabolic, kidney and respiratory diseases is still exceedingly well justified.

The unit has also successfully exploited their discoveries e.g. on innovative biomarkers and therapeutic targets, in order to deliver better prevention and patient care. On the whole, the establishment of C2VN has created substantial added value for the participating teams inasmuch as more of them benefit from the expertise of hospital platforms managed by C2VN members e.g. high-throughput sequencing facilities, platelet phenotyping, the vascular monitoring platform, including the biology of extracellular vesicles, and the Center for Cell Engineering and Therapy. There is also strong integration within additional national patient associations that have markedly improved the research structures available to the different teams as well as accessibility to patient cohorts.

### Weaknesses and risks linked to the context

The C2VN seems to have the policy of having PIs play to their strengths to pick projects with promise, this has led to a rather diverse set of projects, some highly successful, others less so.

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

#### Strengths and possibilities linked to the context

The unit has set up internal rules concerning human resources management and decision-making, staff working conditions, health and safety, protection of scientific potential and integrity and management of the laboratory's resources.

Gender parity is achieved with a total of 116 women (53%) and 101 men (47%). The director of the unit, the deputy director and the general secretary are women. However for researchers, the number of women who are senior PI's remains lower than that of men. The unit has recently appointed two INSERM 'parity and professional equality' correspondents.

In terms of safety, four members (2 for the PMMS site and two for the pharmacy site) are part of the Health and Safety Committee (H&SC) and the Quality, Health and Safety Group (QHSG). In order to fully comply with the health and safety rules, the H&SC ensures the writing of the consolidated risk assessment document ('DUER') every year and sensitises newcomers to the potential risks and dangers. They have also implemented several certification procedures to secure the technical activities. The H&SC manages the occupational health and safety register and the annual campaign for the identification of individual exposure to chemicals and hazards. Staff participate in psychosocial risk assessment and prevention campaigns and a working group composed of technicians, researchers, PhD students has regular meetings.

Risk prevention: The H&SC is in charge of completing our consolidated risk assessment document ('DUER') every year at both sites (MPMS Faculty and the Faculty of Pharmacy). An action plan is established for the following year to resolve any dysfunction and identify areas for improvement.

A data protection policy has been set up (secure IT system and computer storage with double daily on-site backup and external storage spaces) and on site security measures are in place (secure access to premises by badge).

A business continuity plan has been set up during the first wave of the SARS-CoV-2 pandemic and is regularly updated. Psychosocial risk assessment: C2VN has participated in three psychosocial risk assessment campaigns (AMU, INRAE and INSERM campaigns).

#### Weaknesses and risks linked to the context

No specific weaknesses have been identified. But the unit is committed to increasing its efforts to take the following environmental preservation measures (waste sorting, recycling, collection of data necessary for the realisation of the assessment of greenhouse gas emissions (EGGES), and energy recovery). It has so appointed a member of the INRAE staff as 'Relais Développement Durable'.

## EVALUATION AREA 2: ATTRACTIVENESS

#### Assessment on the attractiveness of the unit

The attractiveness of the unit is outstanding-based, on the quality of the platforms with a translational impact for the projects, the organisation of international scientific events, the mobility of basic scientists with permanent position (n=3), the quality of hosting policies for students with thirteen European training grants and half of the PhD students who defended their thesis during the last mandate have obtained a position, grants for projects obtained from ANR (n=17), RHU (n=8), many foundations such as 'Fondation de France, Fondation pour la Recherche Médicale, Société Française du Diabète' grants from Amidex (n=10), national PHRCs (n=29), creation of a start-up (n=1). In spite of a fair number of applications to ERC, they were not granted.

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

#### Strengths and possibilities linked to the context

All C2VN teams have largely supported the organisation of excellent national and international scientific events (49) during 2016–2021, with more than twenty international conferences in which C2VN researchers were members of the organising committees such as the organic World conference 2021: organisation and Chair of the scientific workshop on 'Sustainable Organic food system) and the fourth European Congress of Thrombosis and Haemostasis, Ghent, for example.
Members of the C2VN have participated on editorial committees of 40 journals.
The unit includes members of international learned societies (International Society Thrombosis and Haemostasis (ISTH), Member of the Task Force of European Society of Cardiology (ESC) for the drafting of the European Guidelines or elected member of the board of atherosclerotic group and Interventional Cardiology of the ESC as example). At national level, many C2VN members are involved in learned societies or are members of scientific institutions (Scientific committee of Fondation de France, Scientific committee of 'Société Francophone du Diabète' (SFD), Scientific committee of the SFN (Société Française de Nutrition).

They planned to organize16 laboratories together around the 'Institut Phoceen du Coeur et des vaisseaux', with the objectives to understand the physiopathological mechanisms involved in the interaction of vessels/blood. The aim of this 'AMU institute' if it is granted by AMU should be to repair the cardiovascular system by engineering.

#### Weaknesses and risks linked to the context

During the evaluation period, C2VN did not have any ERC or members at the IUF.

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

#### Strengths and possibilities linked to the context

The attractiveness of the unit is evidenced by the number of academic staff who recently joined the unit (at least 3 permanent basic scientists during the last mandate, together with young and senior researchers who have been recruited by competition. The unit has also welcomed several visiting senior scientists (Russia, Argentina, Pakistan) and medical doctors from foreign countries (Mexico, Guatemala)
The quality of the hosting policy for students included doctoral students' club and a student day during which doctoral students and Master students can present their project work.
Half of the PhD students who defended their thesis during the last mandate have obtained a position. Further scientific collaboration and an even closer networking would, however, be expected if the teams were physically integrated into a unit in a single physical space.

The policy regarding open science allowed deposition of nearly all of the articles published by members of the unit in the HAL open database in recent years
The policy for science integrity included compulsory training courses on research ethics and on scientific integrity set up at the Aix Marseille university level. Of note, these two training courses must be validated by students to start their PhD.

#### Weaknesses and risks linked to the context

No specific policy seems to be dedicated to the postdoctoral fellows (e.g. language courses or specific methodological training) which may explain the relative low numbers of postdocs (11) welcomed during the period.

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

#### Strengths and possibilities linked to the context

The unit participates in thirteen European programs, two of which it coordinates (contracts EUTOX and Italian multidisciplinary group on syncope). These programs include two PhD programs with industrial partners TICARDIO and STRATEGY-CKD, IMI CARDIATEAM, two ERANET programs (BIO-Belief and INTEGRActiv), Hub of knowledge SYSTEMIC (funded by JPI HDHL, FACCE and OCEANS).

It has conducted a total of 46 projects with national funding, of which as PI for six projects funded by the ANR and for six national PHRC. The unit is involved in 29 structures and projects funded by the PIA, eighteen of which it coordinates. Finally, the unit participates since 2017 in a total of 187 funded projects, of which 123 as PI, and received for them a total of 15,938 K€.

C2VN has several opportunities to further develop programs supported by national or European funding thanks to its enrichment in technical expertise platforms with specific new equipment, a capacity to attract industrial partners notably through two innovative therapeutic strategy programs

#### Weaknesses and risks linked to the context

There is currently a lack of technical and administrative staff that necessarily impacts the dynamism of the unit, especially to respond to various large national and international competitive calls. Finally, there is a risk of not being able to recruit young researchers on a permanent basis in order to boost research and bring in new expertise.

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

#### Strengths and possibilities linked to the context

The unit benefits from easy access to expertise and cutting-edge technological resources with its four technical platforms (BIOMET, PhenoMars, AMUTICYT,PIVMI and CERIMED) which have the label 'Technological platforms of the Aix-Marseille site' and in addition the hyperbaric platform. This label gives the platforms visibility and allows them to answer calls from the A*midex Foundation. The platforms are managed by qualified scientific and technical staff.
The platforms are open to academic and private communities. The services are used to finance their infrastructure, their maintenance, the renewal of small equipment and to hire non-permanent staff.

#### Weaknesses and risks linked to the context

Platform resources are not always sufficient to allow the acquisition of very large equipment that is purchased via institutional calls (PIA, Equipex) and in the future (HIPE Equipex + for EchoMRI (A*midex, Region Sud).

## EVALUATION AREA 3: SCIENTIFIC PRODUCTION

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

The publication output of the C2VN as a whole is excellent with high levels of production and an improvement in comparison with the last mandate (increase of 15%). 414 original papers (34% of the total number of publications – has been published as strategic positions (first, last position, or corresponding author). Significant papers (11%, n=135) were published between the teams. In the whole, 66 (16%) are in the top-level journals (*Nat Commun*, *PNAS, Nat Genet, Science Translat Med, Lancet, New Engl J. Med, JAMA Cardiol)* but some teams only published in specialty journals.

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

#### Strengths and possibilities linked to the context

From 2016 to 2021 C2VN has produced 1231 publications including original articles, reviews, letters/comments, and editorial pieces (without redundancy between teams). More than 60% of the output corresponds to the most internationally renowned journals of theirs disciplines
and more than 85% in the leading specialised journals. Of these, 52 (4%) are highly cited papers, and 414 (34%) original articles (excluding reviews and letters) correspond to team output in strategic positions (first or last position), of which 66 (16%) are in highly quoted journals (1 *Nat Commun*, 3 *PNAS, Lancet (1 review and 2 letters)* and several more in the framework of international collaborations *(4 Nature Commun, Nat Sustainability, Nat Genet, Science 1 Translat Med, 3 Lancet, 5 Lancet.*

#### Weaknesses and risks linked to the context

There are stronger and weaker teams in the Unit. A more detailed analysis of how the Unit could react to increase output in some of the teams rather than just increasing the number of teams was lacking.

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

#### Strengths and possibilities linked to the context

Production appears to be globally linked to the size of the teams.
More than 60% of the output corresponds to the most internationally renowned journals of theirs disciplines and more than 85% in leading specialised journals. Importantly, C2VN has produced several general-science articles in a strategic position (first or last position) (1 *Nat Commun*, 3 *PNAS* and *Lancet* (1 review and 2 letters)) and several more in the framework of international collaborations (4 *Nat Commun, Nat Sustainability, Nat Genet,* 2 *Science Sci Translat Med, PNAS, New Engl J. Med,* 3 *Lancet, 5 Lancet (specialities), JAMA Intern Med, JAMA Cardiol* x 2, *JAMA Oncol).* The unit has numerous highly cited papers.
When analysing team by team:

Team 1 (expertise on micronutriments) has published 254 original publications, 27 reviews and five letters or editorial material. PhD students have authored 21% of publications (N=60).

Team 2 members (haemostasis and venous thromboembolism and chronic airway disorders) has published 206 articles and are in 79 original articles and fourteen reviews as first or last position (with 83% of original papers are in the first or second quartiles) and in 28 papers in second or penultimate position. Of note, many of these articles have been cited more than twenty times. 127 original papers correspond to collaborative work, of which 41% from international collaborations.

Team 3 (pathophysiology of endothelium) produced 151 original publications, 21 reviews and two book chapters. The team published 85 original papers, twenty reviews and two book chapters, in which the first and last or corresponding author were members of the team. 113 original articles (75%) were published in journals of the first quartile, and 30 (20%) articles were published in journals of the second quartile.

Team 4 (CD146 molecule) has published 228 articles, more than seven per full-time researcher, among which 73 articles as first or last position, balanced between clinical and basic science. Among these publications are sixteen reviews or guidelines, and 150 collaborative papers.

Team 5 (adenosinergic system in cardiology) has published 247 articles, with 119 with a team member in the first or last position, and 47 from international collaborations.

#### Weaknesses and risks linked to the context

While the scientific output is generally strong, some of the teams publish mostly in subspeciality journals rather than more general journals with high influence. This issue was recognised by some of the teams and listed in the report.

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

#### Strengths and possibilities linked to the context

The doctoral school imposes two courses, one on ethics and the other on scientific integrity. Attendance at these courses is mandatory to be allowed to defend the doctoral thesis.
Since 2019, Team 3 has developed the use of the electronic laboratory book to ensure traceability and reproducibility of results and the unit wishes to extend this use to all teams.
The unit has established common rules for the signing of scientific publications.
To promote open science, the deposit of all publications in HAL's open archives is encouraged and in agreement with co-authors and publisher policy.

#### Weaknesses and risks linked to the context

A cell or working group to raise awareness of scientific integrity is not established in the unit.

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

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

Altogether, the Unit shows an outstanding level of product development, notably those intended for the medical world. The unit has obtained a lot of industrial partnerships (42 R&D contracts, 4 licenses, creation of 1 start-up, 5 CIFRE contracts and 2 industrial contracts for the PhD students) and have filled 25 patents. The unit has coordinated 35 cohorts of patients as PI. They have participated in 111 clinical trials and 29 PHRC (15 as PI). They made fifteen declarations of invention, applied for 25 patents and four patents were licensed.
The entire team of the unit has a lot of interaction with civil society on a regular basis (every year), through:

i) its participation in scientific presentations dedicated to the public,
ii) its participation in meetings with various patient associations,
iii) its activity as members of the Nutri'In Med association, which raises awareness of the relationship between health and nutrition.

The unit uses media such as

i) television programs,
ii) radio programs
iii) and mainstream journals.

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

#### Strengths and possibilities linked to the context

The unit has developed several long-lasting partnerships with non-academic public health actors and leading companies in the fields of agri-food, pharmaceutical and biotechnology. These projects concern environment- and human-adapted food productions, new techniques to detect and treat thrombosis and bleeding, vascular imaging and regeneration strategies, and preventive or curative treatments for cardiac, pulmonary and vascular consequences of environmental, therapeutic or nutritional stress. Thus, this unit works with 63 industrial partners involving its five teams, including leading companies in the field of *in vitro* diagnostics (ex. Stago, Beckman Coulter), biotechnology (ex. Bioxodes, Idorsia) and pharmaceutics (ex. CSL-Behring, Novartis). These collaborations were possible thanks to the quality of technical platforms and bio-clinical expertise in thrombosis and bleeding disorders of the C2VN.
Moreover, the unit has coordinated 35 cohorts of patients as PI (platelets disorders, haemostasis (MARFAST, Martha, …), France-coag, CRPP (centre de reference pathologies plaquettaires hereditaires), kidney disease (CKD-rein – s, cardiac diseases (GMDICO), …). The collaboration of C2VN with patients is important, in particular through expert patients involved in several therapeutic education programs coordinated by members of the unit, and a close relationship with national patient associations such as the AFH (Association française des hémophiles) via the FranceCoag network supported by the DGOS and the rare disease reference centre for inherited platelet pathologies.

#### Weaknesses and risks linked to the context

The unit has difficulties in maintaining a sufficient and stable administrative staff that could be devoted to the partnerships to be developed with industrial and associative actors.

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

#### Strengths and possibilities linked to the context

The Unit has several long-lasting partnerships with the socio-economic world in the fields of agri-food, pharmaceutical and biotechnology. This led to the development of products, particularly for the medical world, including new techniques to detect and treat thrombosis or improved vascular imaging and vessel regeneration therapeutic strategies.
More specifically, the Unit has filled thirteen invention declarations and 25 patents, four of them being licensed by companies.
The unit has participated at 111 clinical trials and 29 PHRC (15 as PI). Moreover, one start-up has been created within the framework of the C2VN: Remedex was created in 2020 and provides services and tools to enable physicians to perform injections of autologous platelets under rigorous medical and scientific conditions.
Finally, the Unit technical platforms are open to private partners and provide relevant services to the socio-economic world. Moreover, some teams develop innovative tools in partnership with industrials (Hybrigenics services, BioCytex, Stago).
A start-up emergence project is underway. Finally, C2VN is expected to collaborate with the CISAM structure, which is coming to the Timone campus, to promote partnerships with industry.

#### Weaknesses and risks linked to the context

Only a small portion of the patents have been licensed. The development of products for the food industry may be improved.

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

#### Strengths and possibilities linked to the context

The entire C2VN team has a lot of interaction with civil society on a regular basis (every year), though:

- **i)** its participation in scientific presentations dedicated to the public («le grand forum santé», La Provence, La Fête de la Science, La Nuit des Chercheurs, Le Salon International de l'Agriculture, Nutr'in Med congrès as part of Marseille Provence gastronomy, with the association «Les Petits Débrouillards» : the scientific festival, the sport/health festival or world congress of nature, the 'Café des Sciences', science festival 'Pinte of Science'),
- **ii)** its participation in meetings with various patient associations (French Association of Haemophilia and pulmonary embolism, platelet disorders and venous thrombosis, patient associations devoted to scleroderma, thrombotic microangiopathy and vasculitis, chronic kidney disease and scleroderma)
- **iii)** its activity as members of the Nutri'In Med association, which raises awareness of the relationship between health and nutrition.

It also uses media such as

- i) television programs (Allo Docteur, Atout Santé, France 3 «Un Dimanche en Politique, Télématin, émissions France 5, France Info, RTS1 Switzerland, AP-HM Channel, LCM TV),
- ii) radio programs (Radio Bleue, Radio France International, France culture, France Bleu),
- iii) mainstream journals (Top Santé, La Provence, Madame Figaro, La Marseillaise, Le Monde), specialised journals (Nature Sciences Santé, INSERM Magazine, INSERM Actualités, ECO Journal) and various websites (YouTube, Synadiet, mediscoop.net, diabetologie-pratique.com),
- iv) and social media (C2VN Twitter and LinkedIn).

Finally, each year, the unit welcomes pre-baccalaureate students as part of their discovery of the world of research. The unit participates in 'Fête de la science, La Semaine du Cerveau', job fairs organized in middle and second schools, 'Journée Portes Ouvertes des Laboratoires de Recherche' during 'Research Day' organized by the Faculty of Pharmacy and at the Declics operation ('cercle FSER').

#### Weaknesses and risks linked to the context

No specific weaknesses have been identified.

# C – RECOMMENDATIONS TO THE UNIT

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

The Unit should consider streamlining projects more to enhance collaborative potential rather than continually drifting off in all directions. This is likely to be an important consideration following the restructuring of the current five teams into seven teams in 2024 and the addition of groups focusing on topics other than micro-nutrition, the endothelium and the haemostasis.
The unit should be relocated to one physical location to ensure better scientific and organisational interaction.
The unit should continue to develop inter-team projects and expand scientific strategic meetings.
As far as its staff is concerned, too many common tasks are handled by a limited number of permanent ITAs. These tasks should be better distributed among all permanent ITAs, contract ITAs and students.

## *Recommendations regarding the Evaluation Area 2: Attractiveness*

European attractiveness will also require attracting more senior and junior researchers, and international postdocs.
The unit should optimise communication between the teams and personal by also involving the technical staff in the scientific meetings.

## *Recommendations regarding Evaluation Area 3: Scientific Production*

The unit is encouraged to increase the number of publications in highly influential generalist journals when possible. The unit should continue to publish at these high levels.

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

C2VN has several opportunities to strengthen this Area 4, including the development of expert patient cohorts for participating science, a private-public partnership from production to alimentation via the AP-HM, and the proximity of the CISAM (Cité de l'Innovation et des Savoirs d'Aix Marseille).

# TEAM-BY-TEAM ASSESSMENT

**Team 1:** Human micronutrition

Name of the supervisor: Mr Patrick BOREL

## THEMES OF THE TEAM

Team 1 has internationally recognised expertise in the field of lipid micronutrients and lipids. More specifically, they develop models and tools to study the fate of lipid micronutrients and lipids from their sites of digestion/absorption to their sites of action, in order to understand their physiopathological effects. Team 1 has also established strong expertise in metabolomics and coordinates the French registry on hypercholesterolaemia with the objective to better prevent cardiovascular risk.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

As recommended, the team made a special effort to recruit postdoctoral fellows, leading to the recruitment of three postdocs in the last two years.
The management of life in the team has been formalised and includes a monthly meeting with all members, and weekly meetings per research theme. The monthly meetings discuss science issues before broadening out to talk about the team budget and administrative issues, and includes a discussion with the technical staff.
Following recommendations, the team increased its international teaching activities thanks to its involvement (since 2020) in an international Master's program (the International AgroSciences Masters course at Avignon University). In addition, the international curriculum of the Master's program on Biology and Health at AMU is now led by two members of the team, thus reinforcing the team's position in terms of international teaching.
The team also followed the recommendation to reduce the number of projects – which have decreased from fourteen to eight, with in particular the non-renewal of projects without regular funding. Moreover, these projects are now part of three research themes:

1) Lipid micronutrients (LM) and lipid absorption (with 2 projects),
2) Phenotypic and molecular impact of LM on metabolic pathways in adipose tissue (with 3 projects),
3) and a cross-cutting research theme on optimised nutritional approaches to improve LM status and health effects (with 3 projects).

The team also specifically considered increasing its focus on diet sustainability and nutritional security, as suggested, via its cross-cutting research theme that has involved most of the team's researchers and that has secured substantial funding (ERAnet, ANR and, INRAE Metaprogram).
Finally, following the recommendation to enhance the interaction with the other teams in nutritional studies, several projects have been developed and/or are currently ongoing, including a project on cardiac development with new incoming team 7 (next mandate).

# WORKFORCE OF THE TEAM

| **Permanent personnel in active employment** | |
|---|---|
| Professors and associate professors | 5 |
| Lecturer and associate lecturer | 9 |
| Senior scientist (Directeur de recherche, DR) and associate | 5 |
| Scientist (Chargé de recherche, CR) and associate | 1 |
| Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées) | 1 |
| Research supporting personnel (PAR) | 9 |
| **Subtotal permanent personnel in active employment** | **30** |
| Non-permanent teacher researchers, researchers and associates | 0 |
| Non-permanent research supporting personnel (PAR) | 2 |
| Post-docs | 0 |
| PhD Students | 15 |
| **Subtotal non-permanent personnel** | **17** |
| **Total** | **47** |

# EVALUATION

## Overall assessment of the team

The team is excellent with respect to the quality of its publications, its international reputation, its expertise in micronutrients, the presence of two platforms (BIOMET and PhenoMars) which developed a budget model (CRIBIOM) with the industrial partners, its strong interaction with industry, its study from preclinical models to clinics: clinical samples (bariatric surgery) with its leadership in five cohorts. There are only few postdocs but from the grants obtained by the team in 2022, they will hire three postdoctoral fellows. There are two declarations of invention and one patent filled. There are a limited number of publications in generalist journals.
Because of the platforms, the team has collaborative projects with all the teams of the unit.

## Strengths and possibilities linked to the context

**Team 1** has an internationally recognised expertise in the fields of bioavailability, metabolism and metabolic effects of lipidic micronutrients and lipids (notably cholesterol). Its strengths are notably:

i) a leadership position, at the national and international levels, in the field of lipid micronutrients and lipids. The team is involved in the hub SYSTEMIC (JPI HDHL 2020-23), which comprises 42 laboratories from eight European countries, and lead the Nutrition WP hub, which aims to evaluate the relationship between nutrition and climate change

ii) Research on nutrition offering large options for securing private funding (CriBiom, INRAE, Biomeostasis, collaborative ANR).

iii) Two platforms are hosted by the team: Platform BIOMET and PhenoMars. These partnership research platforms received the AMU label attesting the high quality of the technological service built on strong academic skills.

iv) Strong interactions with industrial partners (Biomeostasis, Lactalis, Valorex, Naturex, Tereos, IRSN, Terrena Innovation,,…) via long-term collaborations and platform activities.

v) Researchers (14) and clinicians (7) with complementary expertise in the same team
vi) Numerous cellular and preclinical models, together with access to human cohorts
vii) Participation to international networks and Master program

It is to mention that team 1 has made several major scientific achievements. They reported a new paradigm of vitamin D metabolism by demonstrating that ABCB1 plays a major role in vitamin D excretion by the intestines (Faseb J. 2019 as PI); a novel insight into the role that the microbiota plays in venous thromboembolism which represents a major scientific achievement in terms of biomarker identification (ATVB 2020 as PI); the sex-dependent metabolic phenotype associated with vitamin D deficiency alone or in combination with a high-fat diet, which paves the way for further research concerning epigenetic regulation associated with this phenotype (Faseb J. 2020 as PI); The management of REFERCHOL (the familial hypercholesterolaemia cohort). REFERCHOL offers the team opportunities to conduct clinical and epidemiological studies, as demonstrated by several recent high-impact articles In collaboration (JACC cardiovasc Imaging 2021, Lancet 2021, Atherosclerosis 2018).

Team 1 is recognised at both the national and international levels, in the fields of bioavailability, metabolism and metabolic effects of lipid micronutrients and lipids (notably cholesterol). As a result, they are regularly invited to participate in research projects with academic partners or private companies (projects BIO-BELIEF, INTEGRActiv, TomHealth, PAKINAM, ACTA-miRNA…).

During the evaluation period, team 1 published 254 original publications, 27 reviews and five letters or editorial material. Three articles or reviews published by the team are considered highly cited papers. 159 original articles, two letters and six reviews have been published in collaborations. Five of these collaborative publications (in Diabetologia, Diabetes Care) from one member of the team about the CORONADO study are considered highly cited articles.
Twenty-four percent of team publications have been written with international collaborators (Luxembourg, Europe collaborations)

Members have a remarkable activity of partnership with non-academic actors. During the 2016–2021 period, the team established collaborations with companies, such as Biomimetic, Microphyt, Pileje, IRSN and AMGEN (10 projects), and a technical centre (CTCPA Avignon). The team also leads the ANR collaborative project TomHealth (PRCE of ANR), in which involves major participation from IDCAPS and CTCPA Avignon.

The team is also an active member of the Carnot Institute Star, and members participate in the Carnot Institute Qualiment.
During the 2016–2021 period, two invention declarations were filed, in which one dealt with the metabolic effects of a lycopene metabolite and the other dealt with a microbiota metabolite database. The lycopene metabolite declaration was selected by INRAE transfer for a patent, which is currently ongoing. In parallel, INRAE transfer has proposed a grant to finalise experiments to be included in the patent ('prematuration project').

The team currently conducts five therapeutic patient education programs (TPE) validated by the ARS at the Hospital La Conception (ENDO pole):
1) Education of pregnant women with an endocrine pathology: diabetes, obesity, hypothyroidism;
2) Therapeutic education of the type 2 diabetic patients;
3) Therapeutic education of the type 1 diabetic patients;
4) Therapeutic education of the obese patients;
5) Therapeutic education of patients with pituitary pathologies.

Members of the team frequently participate in scientific presentations dedicated to the general public. They also participated in several TV and radio shows and frequently publish articles in journals and websites dedicated to the general public.

The team has trained 29 students during the last mandate and two HDR were defended.

### Weaknesses and risks linked to the context

The team has difficulties to recruit foreign postdoctoral fellows.
There are a limited number of publications in generalist journals.
There is only from three JPI funded programs as partners as EU grants.

## RECOMMENDATIONS TO THE TEAM

We encourage the team to publish in large audience generalist journals.

**Team 2:** Thrombosis, platelets and vascular disorders

Name of the supervisor: Mrs Marie-Christine ALESSI and Mr Pierre MORANGE

## THEMES OF THE TEAM

The team 2 combines research on haemostasis, platelets, thrombosis and vascular risk.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report already highlighted the high quality research of this team. As recommended, it has continued this trend and has returned a total of 79 original publications between 2016 and 2021, for 24 researchers, ten PhD students and five postdocs: 83% of the original productions were published in journals in the first quartile (60%) or second quartile (23%). The previous evaluation committee had recommended securing long-term funding and obtaining European funding. An effort was undeniably made with the coordination of two ANR programs, a PIA program (BioFit) and a WP1 of a PIA program (RHU Innov CKD). Moreover, the team is involved in two ANR programs and several PHRCs.
The development of European and international research is probably more modest even if the team 2 is involved in several projects like ITN Ticardio and the European IMI Cardiateam project. A Peridot PHC support was obtained to collaborate with Pakistan on hereditary platelet disorders. On the other hand, the team does not appear to have increased its administrative staff, which was previously recommended due to its size.

## WORKFORCE OF THE TEAM

| **Permanent personnel in active employment** | |
|---:|:---:|
| Professors and associate professors | 9 |
| Lecturer and associate lecturer | 5 |
| Senior scientist (Directeur de recherche, DR) and associate | 0 |
| Scientist (Chargé de recherche, CR) and associate | 5 |
| Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées) | 0 |
| Research supporting personnel (PAR) | 7 |
| **Subtotal permanent personnel in active employment** | **26** |
| Non-permanent teacher researchers, researchers and associates | 0 |
| Non-permanent research supporting personnel (PAR) | 6 |
| Post-docs | 5 |
| PhD Students | 10 |
| **Subtotal non-permanent personnel** | **21** |
| **Total** | **47** |

# EVALUATION

## Overall assessment of the team

The team is outstanding thanks to many arguments: quality and high levels of publication, even if there are very few top-ranking generalist journals, quality of research projects, well organisation at the international levels (participation in 2 European contracts as PI), translational research (from clinic to bench and vice versa) with fifteen cohorts of patients as PI, participation at 63 clinical trials, good levels of long-term funding from ANR (n=7 with 3 as PI), PIA (n=2 with 1 as PI), 21 R&D contracts, two CIFRE PhD contracts, nine patents, two declarations of invention and numerous grants from Amidex and French foundations.
Only one minor weakness: there are no senior scientists (DR).

## Strengths and possibilities linked to the context

The team 2 has a clear international visibility and strong connection with international learned societies (ISTH and ECTH). It is a multidisciplinary team with basic and clinical researchers which makes their research in haemostasis rich and transversal with a close link maintained with the specialised medical teams taking care of haemostasis disorders.

Another great strength of this team is the accessibility to unique cohorts in thrombosis and haemorrhagic disease. The team coordinated fifteen cohorts as PI (Marfast, cardiateam, Martha ….).

The team is also well integrated in national (French INNOVTE, FORCE, CRISALIS F-CRIN network) and international (A*STAR Singapore, NIH, University of Texas, Leiden University, Germany) networks facilitating research collaborations.
Several members manage national bodies with missions to create scientific tools such as France Coag national register, and several F-CRIN networks.

Team 2 members (haemostasis and venous thromboembolism and chronic airway disorders) has published 206 articles and are in 79 original articles and fourteen reviews as first or last position (with 83% of original papers are in the first or second quartiles) and in 28 papers in second or penultimate position. Of note, many of these articles have been cited more than twenty times. 127 original papers correspond to collaborative work, of which 41% from international collaborations.

Team 2 has participated to editorial committees of sixteen journals (Journal of Thrombosis and Haemostasis, Cells, Frontiers, European respiratory Society…).

Team 2 has the opportunity to reinforce its explorations by bioinformatics tools thanks to partnerships. The team 2 has also recruited two additional MCU-PH who will consolidate the work on platelet pathologies. New original haemostasis-lung research axes could be created thanks to the integration in the unit of a new expert in lung diseases. Finally, the rapprochement with the cardiovascular institute will certainly encourage new projects on thrombosis. Team members were invited to present their work to the International Society of Thrombosis and Haemostasis (ISTH) and to lead masterclasses. They organised international meetings (European congress of Thrombosis and Haemostasis)
The team has trained 25 students during the last mandate and three HDR were defended. The team has hosted four postdoctoral fellows from Italy, Ukraine, the Netherlands and Sweden.
One member was in the Inserm scientific council (2018–2022) and one member was a member of Inserm CSS3 (2021–2025).

The team received international grants as partner (A*STAR Singapore, NIH) and small funding as PI (ISTH small grant). They received European grants as partners (IMI-H2020, ITN Ticardio grant, ANR, bilateral call Germany/France, Leiden University).
They obtained seven ANR grants with three as PI, two A*midex grants, one AAP maladies rares, impasse diagnostique and one AO Carnot star. The team also obtained grants from 'Fondation de France' (x2), 'Fondation pour la recherche médicale', 'Fondation maladies rares', 'SFD (Société francophone du diabète)', 'Fondation de recherche en santé respiratoire, "Fondation du osiuffle (X2)"
One member of the team has won several prizes (FRM, F. Patay prize in 2016) and the European respiratory Society in 2018.

### Weaknesses and risks linked to the context

The team 2 has no senior full-time researchers only CRCN INSERM researchers (n=5) and relatively few publications to high-level generalist journals that could impact its public image (comment of the previous evaluation). The objective of recruiting an already known researcher in the bioinformatics field was not achieved.
The research's quality and expertise of team 2 significantly reduce threats of failures.' However, turnover and instability of expert non-permanent positions could lead to a loss of key technical competences.
The difficulties to recruit postdoctoral fellows could alter the quality and dynamism of the research. The absence of a permanent data manager could reduce the capacity to secure methodological work.

## RECOMMENDATIONS TO THE TEAM

There is still an improvement in areas to be performed such as artificial intelligence, bioinformatics and mathematics, although the team's engineers are trained in these areas.

**Team 3:** Endothelium, Circulating Cells and Vascular Pathologies

Name of the supervisor: Mrs Françoise DIGNAT-GEORGE and Mr Christophe DUBOIS

## THEMES OF THE TEAM

Team 3 has internationally recognised expertise in the pathophysiological mechanisms that regulate vascular homoeostasis. Its strengths are top-notch skills in intravital microscopy applied to *in vivo* models of thrombosis and inflammation, and a leadership position in the biology of extracellular vesicles and the development of technological solutions dedicated to their detection and functional characterisation.
This team has been a pioneer in the field of noninvasive biomarkers and biotherapies addressing vascular disorders. This continuum from identification of new molecular targets to standardisation studies and related guidelines supported by international networks allows team 3 to emerge and deploy new strategies for personalised vascular medicine.
During the past contract, Team 3 focused on interactions between blood cells and endothelium in immunothrombosis and cancer, extracellular vesicles in vascular homoeostasis and disease and innovative strategies for vascular regeneration, in terms of monitoring and biotherapies.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Team 3 has strived to maintain its high educational level (17 PhDs defended a thesis during this contract, with at least two publications in first position) and ensure a continued high standard of publications during this contract (about 150 publications of which 75% were in most prestigious journals).
In addition, two researchers obtained accreditation to supervise research (HDR) and developed their own projects, as attested by their record of publications in senior positions, one in PNAS and one in Blood, invited conferences and their own national collaborations and international connections.
Some team members take part to the subcommittee for standardisation (SSC) in vascular biology of the International Society on Thrombosis and Haemostasis (ISTH) and one member created a European consortium on the topic of thrombosis and cancer.
In line with the HCERES recommendations, team 3 coordinates at the AMU level the ITN with European funding, TICARDIO, to reinforce basic research on thrombo-inflammation and boost translational applications for extracellular vesicles as innovative vascular biomarkers. In partnership with industry leaders in *in vitro* diagnosis and haemostasis, team 3 coordinates the RHU4 project 'Innov-CKD' designed to develop extracellular vesicles as a new economically viable form of biomarkers to identify the risk of bleeding and thrombosis and personalise anticoagulant treatment.
To slim down the number of subprojects and concentrate efforts on projects with high scientific impact, team 3 has narrowed its research theme down to two main foci: the first look into the mechanisms through which immunothrombosis interfaces with endothelium, circulating cells and extracellular vesicles and what this knowledge means for the management of cardiovascular disease; the second concentrates on mechanisms of vascular regeneration based on original imaging strategies in an effort to develop innovative vessel-targeting therapies.

# WORKFORCE OF THE TEAM

| **Permanent personnel in active employment** | |
|---|---|
| Professors and associate professors | 11 |
| Lecturer and associate lecturer | 12 |
| Senior scientist (Directeur de recherche, DR) and associate | 0 |
| Scientist (Chargé de recherche, CR) and associate | 1 |
| Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées) | 3 |
| Research supporting personnel (PAR) | 5 |
| **Subtotal permanent personnel in active employment** | **32** |
| Non-permanent teacher researchers, researchers and associates | 0 |
| Non-permanent research supporting personnel (PAR) | 4 |
| Post-docs | 1 |
| PhD Students | 17 |
| **Subtotal non-permanent personnel** | **22** |
| **Total** | **55** |

# EVALUATION

## Overall assessment of the team

The team is outstanding with an outstanding management based on the balance of academic/industrial collaborations, scientific strategies, leaders in extracellular vesicles field, intravital models of thrombosis. The team has an international visibility, many patents (8, with 5 shared with team 4)) with valorisation, development in the platform of intravital microscopy for which they are pioneers. They have started to develop deep learning. The whole of the team obtained a lot of grants (2 PIA with 1 as PI, AMIDEX (n=3), fourteen PHRC with 6 as PI) but no ANR grants as PI. Every member of the team published in top rank journals of the specialities (Blood) and generalist journals (PNAS). They have difficulties to recruit foreign postdoc fellows. They have created a start-up (REMEDEX) during the last mandate and obtained fourteen R&D contracts.

## Strengths and possibilities linked to the context

**Team 3** has an internationally recognised expertise in the pathophysiological mechanisms of vascular homoeostasis.
Its strengths are notably: top-flight skills in intravital microscopy applied to *in vivo* models of thrombosis and inflammation; a leadership position in the biology of extracellular vesicles and the development of technological solutions dedicated to their detection and functional characterisation; strong connections with hospital platforms for vascular monitoring, imaging and cellular bioengineering, access to biobanks and clinical studies; supervision of three platforms (PIVMI, AMUTICYT and CERIMED) that favours translational research.
Members have a permanent link with SATT Sud-Est and incubators to valorise research; a strong connection with industrial partners to be named here to ensure bench to bedside research; medical innovations in the field of new noninvasive biomarkers and biotherapies addressing vascular disorders.

They are leaders in standardisation studies and related guidelines supported by international networks to be named

It should be mentioned that team 3 has made several major scientific achievements. They reported the role of polymorphonuclear cells in immunothrombosis (in particular regarding thrombosis associated with cancer), thanks to the team's expert skills in intravital microscopy to analyse in vivo models of thrombosis and inflammation (PNAS 2021 as PI); the protective function of highly fibrinolytic leukocyte extracellular vesicles, favouring microthrombi dissolution (Blood, 2021) and new functional signatures of microvesicles, which have provided key insight to advance individualised therapy for patients with coagulopathy; the regulatory mechanisms of endothelial progenitor cell regeneration in vascular inflammatory diseases, which has led to the development of innovative vascular imaging and biotherapeutic strategies in the field of regenerative vascular medicine; new imaging strategies to monitor vascularisation and target the endothelial permeability response, combining team 3 expertise in endothelial pathophysiological responses and PET imaging (PNAS 2018 as PI); the characterisation of the molecular signature of endothelial progenitor cells in the stromal vascular fraction from scleroderma patients and identification of potential therapeutic targets to control the angiogenic and antifibrotic potential of this new cell therapy product; significant advances to understand Covid-19 cardiovascular complications with eleven articles on the subject, including two highly cited publications (PNAS 2020).

Team 3 coordinated the RHU Innov-CKD project (https://c2vn.univ-amu.fr/rhu-innov-ckd) thanks to a patent licensed in partnership with Diagnostica-Stago. The WP2 aimed to develop an automated assay to measure endothelial-derived procoagulant and fibrinolytic extracellular vesicles.

Team 3 has obtained a European grant, TICARDIO (https://ticardio.eu), based on cooperation between three excellent international research Centers for Thrombosis and Haemostasis (Germany and Netherland). This program aims to elucidate the multifaceted mechanisms involved in thrombo-inflammation and constitutes a great opportunity for team 3 to recruit a new generation of international PhD students with access to innovative educational programs linked with industry partners.

Besides, Team 3 has raised numerous other funds, including national ANR as partners, APHM and 'Programme Investissement Avenir' of the French government, as well as associations and industrial contracts (POIETIS, Diagnostica Stago, Bioxodes, Roche,…). It is to mention that the team has established several long-lasting partnerships with leading companies in the fields of haemostasis and *in vitro* diagnostics, biotechnology and pharmaceutics. Team members also participate to 25 clinical trials.

Team 3 has an excellent activity in terms of scientific production. It published 151 original publications, 21 reviews and two book chapters, in the best journals of the speciality. One hundred and fourteen original articles (75%) were published in journals of the first quartile and 29 (19%) in Q2. In 86 cases (57%), a member of the team was the first, last author or corresponding author.
Thirty-five percent of publications (35%) were produced with two or more of the C2VN teams; Thirty-three publications (22%) were with international teams (Germany, Netherland).
A further strength of the team is its high educational level with 35 PhD students trained by the team during the past contract, with a good equilibrium in the repartition of the directions between team members. Of note, 86 publications were signed in the first or last position by the PhD students (61% of the production). Seventeen students have already obtained their PhD, and eleven students have obtained permanent positions as (associate) professors with hospital duties (including at Harvard Medical School/Beth Israel Deaconess Medical Center).

Three former students have postdoctoral positions abroad, one student is now a temporary engineer in the team, and two former students are currently working in private companies. Seventeen students are currently carrying out their PhD. On average, students have completed their PhD with three original articles and two reviews (first author position). Team 3 is also involved in programs of training.
Team members play an important role in various international networks such as ISTH Scientific subcommittees (SSC) Vascular Biology and SSC in Haemostasis and Malignancy. They are also involved in the European Network European Vascular Biology Organization and the European Thrombosis and Haemostasis Alliance.
Team 3 has produced three declarations of invention and has ten patents (3 at the international), some of them in collaboration with Team 4. Importantly, two members of the team created the start-up Remedex in 2020 to provide services and tools to enable physicians to perform injections of autologous platelets under rigorous medical and scientific conditions. It is currently expanding at the national level with job creations.

### Weaknesses and risks linked to the context

The team has difficulties to recruit foreign postdoctoral fellows.
Team includes two permanent Inserm research scientist and five research engineers (3 university and 2 INSERM).

## RECOMMENDATIONS TO THE TEAM

The team should recruit permanent basic scientists and apply to more academic funding (such as ANR) as PI.

**Team 4:** Novel endothelial molecular targets

Name of the supervisor: Mr Stéphane BURTEY and Mr Marcel BLOT-CHABAUD

## THEMES OF THE TEAM

Team 4 has the title *New Molecular Endothelial Targets* but really focuses on only two molecules i.e. the aryl hydrocarbon receptor (AhR) and CD146, also known as melanoma cell adhesion molecule (MCAM). The latter is a membrane glycoprotein and member of the immunoglobulin gene superfamily normally expressed by vascular endothelial cells, smooth muscle cells, and pericytes. Team 4 is one of the few groups that have focused so intensely on CD146 and they are considered THE experts in this field. The focus on AhR evolved from the team's work on the cardiovascular consequences of tryptophan-derived uremic toxins, which activate AhR and they are aiming to discover how that activation leads to thrombosis.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was encouraged to continue its strong publication record and to explore interactions with the lay public (media) as well as to continue its strong profile in teaching. The team was also encouraged to recruit full-time researchers during the funding period. The team addressed these points by participating in the 2020 Pint of Science festival and in the 'Société Francophone de Néphrologie, Dialyse et Transplantation (SFNDT)' webinar during the first wave of the Covid pandemic. This step provided interaction with journalists. Team 4 also now participates in an ITN with European funding, STRATEGY-CKD. However they have not been successful in increasing the number of full-time researchers.

## WORKFORCE OF THE TEAM

| **Permanent personnel in active employment** | |
|---:|:---:|
| Professors and associate professors | 6 |
| Lecturer and associate lecturer | 4 |
| Senior scientist (Directeur de recherche, DR) and associate | 1 |
| Scientist (Chargé de recherche, CR) and associate | 0 |
| Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées) | 1 |
| Research supporting personnel (PAR) | 4 |
| **Subtotal permanent personnel in active employment** | **16** |
| Non-permanent teacher researchers, researchers and associates | 0 |
| Non-permanent research supporting personnel (PAR) | 0 |
| Post-docs | 1 |
| PhD Students | 8 |
| **Subtotal non-permanent personnel** | **9** |
| **Total** | **25** |

# EVALUATION

## Overall assessment of the team

The team is very good. They are the international experts on CD146, and have six patents (5 shared with team 3) and very strong collaborations with industries (5 R&D contracts). The team tends to publish in specialised rather than more influential general journals with 29% publications as major authors – reflecting the large percentage of collaborative projects with external PIs. Despite the clear strengths, the project seems to be drifting away from cardiovascular diseases. The same comments applied for the AhR. Thus, while both molecules are really interesting targets scientific projects are not entirely focused on the cardiovascular system which impacts on the integration into the unit as a whole. For the project on biomarkers, there are the same issues on the focus of the unit.

## Strengths and possibilities linked to the context

The innovation strength of this team is evidenced by the seven patents they filed (including three research and development contracts with the option to license) with six shared with team 3 of which one is licensed by Syndivia.
Concerning opportunities, team 4's research on two proteins involved in endothelial health may have major clinical implications and the translation of their results into patient care solutions.

They have successfully developed five projects with industrial partners (MSD Avenir – in a framework agreement with INSERM; Virbac, Biotem and Syndivia – which is a start-up). These programs involve the application of sCD146 as a biomarker of implantation efficacy in *in vitro* fertilisation (Biotem), anti-sCD146 antibodies to prevent fibrosis in chronic renal failure (Virbac), and generation of an antibody-drug conjugate based on a specific tumoral anti-CD146 antibody, which was generated and humanised by the team for applications in pancreatic cancer (Syndivia).
Furthermore, the team members have various backgrounds, a good grasp of the clinical implications of the various pathologies, and access to various cohorts and European networks. They have participated in ten clinical trials as PI. They are involved in seven biobanks as PI (CKD-rein).

The team has participated in three European grants one as PI (EUTOX grants, 2016–2021, 47 K€), H2020 research and innovation (STRATEGY CKD, 2019–2023, 375 K€).

The team obtained 3 ANR grants, one as PI (FIBROTARGET, 2022–2026, 261K€), 4 PHRC 2 as PI (2018–2024, 144K€ and 2020, 40K€), five AORC with 3 junior, one grant from A*midex (2016, 35K€).
They also obtained nine grants as PI from 'Fondation de France', Société Francophone de Néphrologie, Dialyse et Transplantation (x5), 'Fondation pour la Recherche Médicale' and 'Fédération Française de Cardiologie'.
One team member is involved in Management committee of ITN Strategy CKD, two members of EUTOX (2016-ongoing)

The team has published more than 200 articles with 51 at first or last position. Thirty-seven publications are in the top journals of the speciality pas PI such as (Journal of Allergy and Clinical Immunology, Kidney International, Theranostics, Hypertension, J Am Soc Nephrol.). 150 articles are collaborative papers

Members of the team were in the editorial committee of nine journals (European Journal of Clinical Investigation, Biomedicines).
One of the team leaders is in Scientific board of five companies (Bayer, Alexion, Fresenius Kabi, Astra Zeneca, Boerhinger Ingelheim).
The team has trained eight students during the last mandate and two postdocs and one HDR was defended.

## Weaknesses and risks linked to the context

The team has few technicians and they have not been able to recruit researchers at INSERM or CNRS. The team also seems to have a high turnover of non-permanent researchers and technicians, as few are recruited for full-time positions. Increasing administrative responsibility regarding genetically modified preclinical models, and evaluation work will represent a risk to progressively cut into research time.
The team tends to publish in specialised rather than more influential general journals.

# RECOMMENDATIONS TO THE TEAM

The two projects leaders should work more closely together and ensure a main focus on the cardiovascular system/nutrition. The team should recruit basic scientific researchers.

**Team 5:** Adenosinergic System, Dysoxia, Inflammation

Name of the supervisor: Mr Régis GUIEU

## THEMES OF THE TEAM

The scientific program ranges from basic research to clinical research covering the molecular mechanisms of dysoxia and its consequences on the cardiovascular system focused on the dysregulation of the adenosinergic system. This team has also developed a new theme of cardio-oncology.

## CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

According to the last recommendation: 'The team should improve the recruitment of postdocs and improve the capacity to raise funds from Europe, the ANR and the FRM,' this objective has not been reached.

## WORKFORCE OF THE TEAM

| **Permanent personnel in active employment** | |
|---|---|
| Professors and associate professors | 11 |
| Lecturer and associate lecturer | 7 |
| Senior scientist (Directeur de recherche, DR) and associate | 3 |
| Scientist (Chargé de recherche, CR) and associate | 2 |
| Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées) | 2 |
| Research supporting personnel (PAR) | 4 |
| **Subtotal permanent personnel in active employment** | **29** |
| Non-permanent teacher researchers, researchers and associates | 0 |
| Non-permanent research supporting personnel (PAR) | 2 |
| Post-docs | 0 |
| PhD Students | 13 |
| **Subtotal non-permanent personnel** | **15** |
| **Total** | **44** |

# EVALUATION

## Overall assessment of the team

The team is excellent and well recognised in their field, with the development of a new cardio-oncologic group involved in ESC guidelines. One of the objectives of the team is deciphering adenosinergic system with antibodies which are agonists of the receptor. The team obtained grants with industries such as Abbott, with one patent (adenosis) among the five declared and two declarations of invention. They have recruited basic researchers which will strengthen the basic research projects of the team. The development of the hyperbaric platform is the strength of the team. They did not have any academic grants such as ANR or European grants. The clinical studies are remarkable by the leading of three PHRC and their participation to three clinical trials. There is no postdoc fellows.

There is a very high number of publications (280) with 46% at first or last positions, in high rank journals such as Circulation (X2), JAMA Oncology (X2), JAAC, Cardio-onco,…. The team is very attractive for collaborations with the other teams due to its expertise in hyperbaric conditions.

### Strengths and possibilities linked to the context

The team has excellent recognition in the field of cardio-oncology and has made a real breakthrough as they have regularly published several papers in excellent journals in first or last authors (2JAMA Cardiol 2017–2021; two Circulation-2017-2018; JAMA Oncol-2018; J Am Heart Assoc-2020; J. Immunother Cancer-2020; JACC CardioOnco-2021; Radiology-2022). In total, they published 247 articles with 119 (48%) in the first or senior position. In addition, the investigators are also highly recognised as experts in the adenosinergic system using a unique platform to study dysoxia.

The team's relations with the socio-economic world are excellent as shown by numerous collaboration contracts with substantial funding such as the company ABOTT (ADENOSIS antibody) in the context of a PHR as well as the five deposited patents. The team obtained a European funding with the Italian multidisciplinary group on syncope and one grant from A*midex Méditerranée as PI for collaborative projects with 'Barcelona, Firenze, Pisa, Milan, Genoa and Napoli' and have extended collaborations with Karlinska institute, Lund University, Wisconsin University and University of California. The team has also financial support from FRM (40 K€) and from 'Maison du cœur — Cœur et cancer' (300 K€, 2021–2024) as PI.
They have developed international collaborations to establish a cardio-oncology registry with Harvard Medical School and University of California San Francisco.
Two members of the team were editors of two issues of Biomedicines.
The team has trained thirteen students during the last mandate and four HDR were defended. They have developed e-learning for the 'Collège National de Biochimie et de Biologie Moléculaire Médicale (CNBBMM)'.

The team was involved in three clinical trials as PI and they were in charge of the cohort GMEDICO (2,868 patients) dedicated to 'Pronostic cardiovasculaire des patients suivis en cardiooncologie'

One member was President of the French Subaquatic Medicine Society (2020–2021) and another in the Board of the European Society of Cardiology (FESC) (2016–2021). They have organised French Congress of Subaquatic and Hyperbaric (2021) and EuroPCR (2022).
Members have participated to five guidelines (for example, Guidelines for the diagnostic and management of Syncope)
They have participated in public debate on apnoea risk and physiology (FFESSM (Fédération Francaise d'étude des sports sous-marins)) and they have created the gmedico website.

### Weaknesses and risks linked to the context

Fundamental research is modest, which is partly reflected in a lack of finance from projects (ANR, European). The arrival of the CNRS researcher is essential to strengthen this aspect. The *members of the team are frequently invited to national and international congresses (40 national, 9 international)*.

# RECOMMENDATIONS TO THE TEAM

Recruit postdoctoral fellows. Apply to academic French (ANR) and European grants.

## CONDUCT OF THE INTERVIEWS

### Date(s)

**Start:** 21 novembre 2022 à 8 h 30

**End:** 22 novembre 2022 à 13 h

**Interview conducted: online**

### INTERVIEW SCHEDULE

**Day 1 –**

**8:30 a.m.** **Presentation of the committee**

**8:45 a.m.-9:30 a.m.** **Highlights of the Unit by the Director** (25min presentation+ 20min questions)

**9:30 a.m.-10:10 a.m.** **Team 1**: Human micronutrition **LANDRIER Jean-François – REBOUL Emmanuelle**
(20 min présentation : 20min questions)

**10 h 10-10 h 50** **Team 2**: **Thrombosis Platelets and vascular disorders: MORANGE Pierre-Emmanuel — PEIRETTI Franck**
(20 min présentation : 20 min questions)

Coffee break: 3:n 10 p.m. h50-11h05

**11:05 a.m.-11:45 a.m.** **Team 3**: Endothelium, circulating cells and vascular diseases **DIGNAT-GEORGE Françoise – PANICOT-DUBOIS Laurence**
(20 min présentation : 20 min questions)

**11:45 a.m.-12:25 p.m.** **Team 4**: **New molecular endothelial targets: BLOT-CHABAUD Marcel – BURTEY Stéphane**
(20 min présentation : 20min questions)

**12H30-13H30 LUNCH**

**1:30 p.m.-2:10 p.m.** **Team 5**: Adenosinergic system dysoxia and inflammation **GUIEU Régis – THUNY Franck**
(20 min présentation : 20min questions)

**2:15 p.m.-4:30 p.m.** **Committee debriefing (closed doors)**

**DAY 2**

**8:45 a.m.-9 H 00** **Committee debriefing (closed doors)**

**9 a.m.-9:30 a.m. Meeting with technicians and administrative staff (closed doors)**
Contact: Karim Fallague (karim.fallague@univ-amu.fr)

**9:30 a.m.-10 a.m. Meeting with PhDs and postdocs (closed doors)**
Contact: Cléa Dubrou (clea.dubrou@univ-amu.fr)

**10 a.m.-10:30 a.m. Meeting with researchers not team leaders**
Contact: Nathalie Lalevee (Nathalie.lalevee@univ-amu.fr)

Coffee break: 15 mn

**10:45 a.m. – 11:30 a.m. Meeting with the representatives of the local institutions**

10 h 45-11 h 00 : Université de Marseille : Philippe.delaporte@univ-amu.fr
11 h-11 H 15 : Inserm delegate: armelle.regnault@inserm.fr; dr-marseille@inserm.fr
11H15-11H30: Inrae delegate: alimh@inrae.fr ; jean-philippe.nabot@inrae.fr

**11:30 a.m.-11:45 a.m. Closed-door meeting of the committee (closed doors)**

**11:45 a.m.-12:15 p.m. Meeting with the Directors (present and futur)**

**12:15 p.m.-1 p.m. Committee meeting (closed doors)**

PARTICULAR POINT TO BE MENTIONNED

# GENERAL OBSERVATIONS OF THE SUPERVISORS

Le Président de l'université

au

Département d'Évaluation de la recherche - Hcéres

Objet : Observations de l'unité relatives au rapport d'évaluation des experts Hcéres
N/Réf. : VPR/LS/AMS/CM – 23-06

Dossier suivi par : Cécile Merle
Tél : 04 13 94 95 90
cecile.merle@univ-amu.fr

Vos réf :
DER-PUR230022991 - C2VN - Centre de recherche en cardiovasculaire et nutrition de Marseille

Marseille, le jeudi 15 juin 2023

Madame, Monsieur,

Je fais suite à votre mail du 25/05/2023 dans lequel vous me communiquiez le rapport d'évaluation Hcéres de l'Unité de Recherche C2VN - Centre de recherche en cardiovasculaire et nutrition de Marseille.

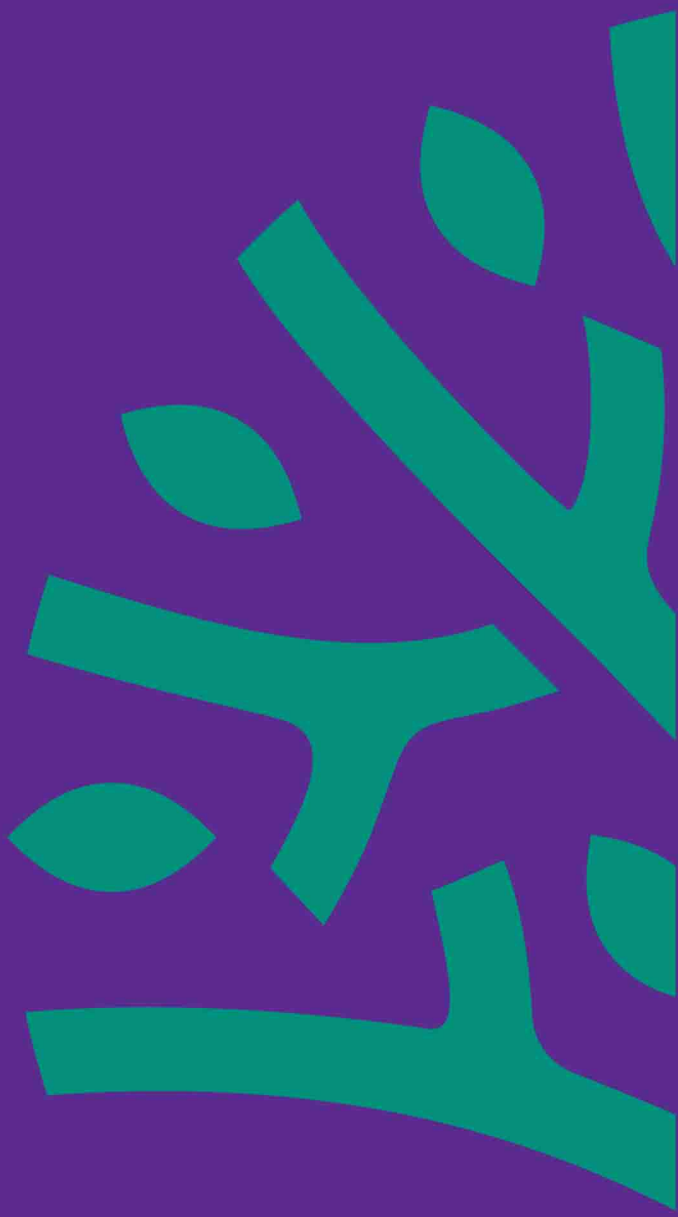
Comme demandé dans ledit mail, je vous indique que les tutelles du C2VN, Aix-Marseille Université, l'INRAE et l'Inserm, n'ont pas d'observation à formuler.

Vous souhaitant bonne réception des présentes,

Je vous prie de croire, Madame, Monsieur, l'expression de mes respectueuses salutations.

**Eric BERTON**

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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