Research evaluation

EVALUATION REPORT OF THE UNIT

LNC - Lipides, nutrition, cancer

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Université de Bourgogne,
Institut national de la santé et de la recherche médicale - INSERM,
AgroSUp Dijon,
Université Bourgogne Franche Comté

EVALUATION CAMPAIGN 2022-2023

GROUP C

Rapport publié le 20/06/2023

In the name of the expert committee[1] :

Maude Le Gall, 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:	Ms Maude Le Gall, Inserm, Paris
Vice-chairperson:	Mr Lucas Jacques Waltzer, CNRS, Clermont-Ferrand
Experts:	Mr Julien Edeline, Université de Rennes 1 Ms Irina Giurgea, Sorbonne Universités Mr Philippe Kastner, Université de Strasbourg Ms Virginie Lafont, Inserm, Montpellier Mr Olivier Meilhac, Inserm U1188 Réunion Ms Carina Prip-Buus, CNRS, Paris Ms Stéphanie Venteo, Inserm, Montpellier

HCÉRES REPRESENTATIVE

Ms Marie-Paule Roth

CHARACTERISATION OF THE UNIT

- Name: Lipides, nutrition, cancer
- Acronym: LNC
- Label and number: UMR 1231
- Number of teams: 8
- Composition of the executive team: Professor Francois Ghiringhelli

SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement

SVE6 Physiologie et physiopathologie humaine, vieillissement

THEMES OF THE UNIT

The unit covers an important number of themes as cancer biology, lung fibrosis, tumour immunology, lipid metabolism and stress, pharmacokinetic and dynamic of apolipoprotein, epidemiology of digestive cancer and haematology, developmental genetic, translational haemato-oncology, clinical research.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The research centre 'Lipids, Nutrition, Cancer' (LNC) is a mixed unit affiliated to Inserm, University of Bourgogne, and AgroSup Dijon. Founder teams of the unit LNC came from INSERM units U498 ('Intravascular lipoprotein metabolism'), U517 ('Cell death and cancer'), and EPI-106 ('Epidemiology of digestive cancers'). The structure was created in 2007. Additional groups from the Life Sciences Faculty, CNRS and ENSBANA joined the unit for the 2007–2011 contract. During the second, 2012–2016 contract, the unit included eight distinct groups. During the last contract 2017–2021, EA4271 GAD headed by Laurence Faivre joined the unit. An ERC team was also created by Lionel Apetoh who established his group in 2017.
All the teams are located on the University Campus of Dijon but in different buildings including the Health Sciences Faculty, the University Hospital (CHU), the Georges-François Leclerc Center (CGFL), the Life Sciences Faculty, and the AgroSup school. All the buildings are within a 10min walk.

RESEARCH ENVIRONMENT OF THE UNIT

The University Campus gathers the Health Sciences Faculty, the University Hospital (CHU), the Georges-François Leclerc Center (CGFL), the Life Sciences Faculty, and the AgroSup school. Some start-up and spin off are associated with the unit. The unit is also in close contact with a platform for early clinical trials (CLIPP2), the Clinical Investigation Center (CIC1432) and the Center of Biological Resources (CRB Ferdinand Cabanne). They are also in connection with the SATT-GE (Société d'Accélération du Transfert de Technologies Grand Est).
In addition to recurrent funding from Inserm and University of Bourgogne, the teams received funds from the LabEx LipSTIC, an ISITE-BFC (Initiative for the ISITE Bourgogne Franche-Comté) and two University Hospital Federations: FHU-TRANSLAD (translational medicine for developmental anomalies) and FHU INCREASE (Integrated Centre for Research in Inflammatory diseASEs).

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

Permanent personnel in active employment	
Professors and associate professors	46
Lecturer and associate lecturer	33
Senior scientist (Directeur de recherche, DR) and associate	6
Scientist (Chargé de recherche, CR) and associate	11
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	10
Research supporting personnel (PAR)	120
Subtotal permanent personnel in active employment	**226**
Non-permanent teacher researchers, researchers and associates	25
Non-permanent research supporting personnel (PAR)	51
Post-docs	12
PhD Students	68
Subtotal non-permanent personnel	**156**
Total	**382**

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

Employer	**EC**	**C**	**PAR**
Université de Bourgogne	60	1	15
CHU Dijon	6	2	62
Inserm	0	15	12
CLCC Georges-François Leclerc	3	9	8
Institut Agro	8	0	6
Employeur privé	0	0	14
Université Bourgogne — Franche-Comté	2	0	0
Autre employeur	0	0	2
CHRU Besançon	0	0	1
Université Paris Descartes	0	0	0
Total	**79**	**27**	**120**

UNIT BUDGET

Recurrent budget excluding wage bill allocated by parent institutions (total over 6 years)	4,313
Own resources obtained from regional calls for projects (total over 6 years of sums obtained from AAP idex, i-site, CPER, territorial authorities, etc.)	5,777
Own resources obtained from national calls for projects (total over 6 years of sums obtained on AAP ONR, PIA, ANR, FRM, INCa, etc.)	34,392
Own resources obtained from international calls for projects (total over 6 years of sums obtained)	9,204
Own resources issued from the valorisation, transfer and industrial collaboration (total over 6 years of sums obtained through contracts, patents, service activities, services, etc.).	0
Total in K euros	**53,686**

GLOBAL ASSESSMENT

The research centre Lipids Nutrition Cancer (LNC), composed of eight teams (380 members), is a leading multidisciplinary translational centre in Dijon. It is financed by Inserm, University of Bourgogne and Agrosup School. Scientists and university teachers are working in close collaboration with clinicians to developed translational projects going from basic to translational research leading to new biomarkers and innovative therapeutic approaches.

The unit produced excellent research publications. 2007 original publication were published between 2016 and 2021 within 692 publications signed as PDC by team members. Most of those publications have a very good international visibility. 96 PDC publication are within the top 10% of citations. These include several publications in generalists and/or highly cited journals such as American Journal of Human Genetics, Blood, Diabetes, Gut, Journal of Clinical Investigation, Nat Commun, Nat Genetics, New England Journal of Medicine, Science Translational Medicine …20% of the publications are in the field of Oncology, thirteen in Genetics & Heredity and 8% Critical Care Medicine, the rest are in biochemistry and molecular biology, haematology, surgery, endocrinology, gastroenterology reflecting the large domain covered by the unit.
The attractiveness of the unit ranges from very good (international visibility) to excellent (fund-raising, training).
The unit's members have been highly successful in obtaining funds with a majority of territorial and national origin (17 ANR,10 INCA, eight national PHRC, 6 inter-regional PHRC…) and several grants from other health-related agencies in addition to many grants from charities (11 from the Foundation ARC and 38 from the Ligue Contre le Cancer).
The success in European calls is still low although one ERC starting grant was obtained (but the PI left the centre). Nonetheless, some teams are coordinators or members in international contracts including Europeans ones (ERA-NET *TRANSCAN2*, H2020 *Solve-RD*, H2020 *CBIG-SCREEN, EJP RARE-ILD, MSCA RISE Discover programs)*. Also, *one ERS*/EMBO and one EU MSCA postdoctoral fellowships were obtained.
While some LNC members received a high number of invitations to contribute to international congresses (Keystone Symposium, European Society for Medical Oncology (ESMO), American Society for Clinical Oncology (ASCO), Federation of European Physiological Societies (FEPS)…), the international visibility of more junior members still needs to be improved.
The LNC has not really demonstrated its capacity to attract new teams coming from outside except for one Hospital Professor (recruited from Grenoble), who took over the direction of one team. An international call is planned. Besides, the unit recruited four Inserm researchers since 2016 and another coming from Paris joined the unit in 2021.
The involvement in research, training and teaching is excellent with 77 members having an HDR (including 21 defended since 2016). The research unit plays a major role in the training of students from the University of Bourgogne. About 80 PhD were defended between 2016 and 2021 (out of a total of 143) but few postdoctoral fellows (27) have been hosted. The proportion of foreign students and post-doc is around 15 and 25%, respectively. The creation of an on international doctoral school (master-doctorate program entitled INTHERAPI for 'Innovative Therapies, Pharmaco-Imaging and Multimodal-Imaging of the University of Burgundy-Franche-Comté) should allow to increase the international visibility of the centre.

The overall functioning of the unit is very good. The unit benefits from very good technological platforms, especially for metabolic & lipidomic studies, NGS and bioinformatics. The unit is currently mutualising the technological resources of all the platforms as a unique UMS with IBISA and ISO9001 certification planned. The unit also mutualises some of its institutional funds for common investments and exploratory projects. While all the teams share a translational objective, the sense of belonging to a unit is not very strong, particularly between teams. The integration of the different categories of personnel (support staff, scientists, clinicians, PhD, postdoc…) in the scientific, managerial, and social life of the unit could be improved. The organisation of the unit revealed weaknesses in communication strategies, not only towards the external world, but also within the unit itself.

The valorisation level of the LNC unit is excellent to outstanding. The interaction with the nonacademic world of the LNC is highlighted by five invention declarations, 23 patents, one software as well as nine open source software and one start-up. Most importantly, the centre has set up more than 40 clinical trials. Several teams also obtained important contracts (around 3M€ in total) with industries (Servier, Iderma, Roche, AstraZeneca).
Communications with the public and outreach activities are essentially organised at individual or team level.
The committee assessed two teams as outstanding, two as excellent, two as very good to excellent and two as very good.
Some teams are brilliant in developing start-ups, others in developing research from basic science to clinical trials, others developed international cohorts or diagnostics.

Overall, the committee rates the LCN as excellent.

DETAILED EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The unit was encouraged to formulate a general scientific strategy – possibly around an area of common interest – that aims at further stimulating interactions between research teams and may help improve external recognition of the LNC research centre.
In response the unit has focused on the development of translational research. Accordingly, the name of the unit is now 'Dijon Center of Translational and Molecular Medicine'. This choice might be detrimental to the visibility of the 'nutrition' axis, which is supported by AgroSup and Dijon history.
Although all the teams are involved in translational or clinical research, the diversity of research theme remains important.
The organisation of the unit in terms of structuring of certain teams should be reconsidered.
Two team leaders were replaced during the mandate and one team (SAPHIR/Epi2THM) was considerably restructured. The organisation of several teams remains complex. Some evolutions are proposed for the next mandate (individualisation of 2 emerging teams from 2 large ones).
In addition, all the permanent technical people were positioned on the platforms so that they can help the teams in development.
A special program/course for PhD students within the LNC should be considered. Attendance of seminars should provide credits.
The LNC is member of the integrated international master-doctorate program entitled INTHERAPI for 'Innovative Therapies, Pharmaco-Imaging and Multimodal-Imaging of the University of Burgundy-Franche-Comté. The students are encouraged to attend the scientific seminars proposed by the unit every Monday.
Using LipSTIC as a model, the LNC should try to engage in additional activities to secure funding for joint projects across units.
The unit obtained additional funding from the SATT and through partnership with small and big pharma. It is not clear how that benefited to the development of joint projects across the teams of the unit.
A concerted effort should be undertaken to obtain more EU funding, which currently is limited
(ERC starting grant, program Transcan, Program H2020).
In addition to support from the FEDER, some teams obtained EU funding. Lionel Apetoh (ex Ghiringhelli team member) was granted an ERC starting grant in 2016. F. Ghiringhelli was granted by the ERA-NET program TRANSCAN2. C. Thauvin team was granted by the H2020 program' Solve-RD'. M. Bardou coordinated the H2020 project CBIG-SCREEN. P. Bonniaud was partners for the EJP RARE-ILD and O. Micheau was a partner for the MSCA RISE Discover programs.1ERS/EMBO and one EU MSCA postdoctoral fellowships were obtained.

B – EVALUATION AREAS

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

Assessment on the unit's resources

The unit benefits from an excellent mix of highly qualified staff from the Inserm, University and Hospital. The unit has recruited three CRCN, one DR and two technicians/engineers with Inserm positions as well as twelve associated professors, four professors and fifteen technicians/engineers with University or Hospital-associated positions. It hosted a very good number of PhDs and a good number of postdoctoral fellows. It benefits from very good technological platforms, especially for metabolic & lipidomic studies, NGS and bioinformatics. LNC researchers have been highly successful with competitive funding at the national and regional levels.
The global unit's resource is excellent ranging from very good to outstanding depending on the teams.

Assessment on the scientific objectives of the unit

The scientific objectives of the unit are very good to excellent. The unit has identified a broad common theme 'translational research' to which the different teams are well committed. The unit has done an excellent work at developing translational research in the different research fields of the individual teams, with a commendable combination of basic research, clinical development, and economic valorisation. The location on different sites does not seem to interfere with the cohesion of the teams dispatched over different buildings but may impact the general cohesion of the unit. The thematic diversity of the unit remains strong.

Assessment on the functioning of the unit

The unit has a very good functioning. Its strength and specificity stand from a strong interaction between the researchers and teachers with the hospital, the Georges François Leclerc Center and the large number of physicians and ARCs. The new head of the unit is very dynamic and positively perceived. The scientific life of the unit is satisfactory, and its atmosphere is generally well appreciated. The unit complies with its institutional requirements. However, intern communication aspects and psychosocial risk management needs to be improved.

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

Strengths and possibilities linked to the context

During the last period the unit has recruited three CRCN, one DR and two technicians/engineers with Inserm positions as well as twelve associated professors, four professors and fifteen technicians/engineers with University or Hospital-associated positions. The recruitment of permanent positions is important thanks to the university and the hospital.
The unit has strong links with the hospital as within the 226 permanent staff, including 120 support staff, around half of the staff is employed by the CHU of Dijon. It has a long-lasting experience as a multidisciplinary research centre combining basic, translational, and clinical research in cancer biology, lung fibrosis, tumour immunology, lipid metabolism and stress, apolipoprotein pharmacokinetic and dynamic, epidemiology of digestive cancer and haematology, developmental genetic, haemato-oncology.
It benefits from a huge expertise in translational research and a great agility to validate their results in clinical trials.
A major force of the unit relies on the quality of the technologies and core facilities proposed to the teams. The unit has made great efforts to mutualise and develop its methodological know-how by creating nine platforms regrouped in a UMS called BIOSAND at the disposal of the members of the unit. The platforms were created in coherence with the scientific objectives of the unit and for the development of translational projects to the clinic.
Thanks to its recurrent resources, high level of success in competitive funding, as well as strong financial support through local PIA initiatives (ISITE & Labex) and regional agencies, the unit has maintained an excellent level of equipment and acquired new state-of-the-art technologies (e.g.: spectral cytometer Cytek Aurora, 10X Genomics…).

Weaknesses and risks linked to the context

One drawback of the local recruitment policy with the university and the hospital is that there are only a few full-time researchers and most PI have important teaching and hospital duties.
In addition, despite the asserted will to converge towards translational research, the multiplicity of scientific themes is not reduced, which may hamper the investment policy of the unit. Also, the positioning/independence of the different local platforms, for example between the unit or the CGFL, is not very clearly established.
Unfortunately, the ISITE BFC project was not reconducted in 2021 and there are some uncertainties about the funding coming from the LABEX. The resulting decrease in local resources is a major threat for the unit, in particular for some teams.

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

Strengths and possibilities linked to the context

The objective of the unit is the development of translational research in the different research fields of the teams. The large number of physicians involved in the research of the different teams and the leadership of physicians in many teams underline the commitment to this translational research development. Many members of the UMR have strong connections with clinical research and interconnections with CIC, early clinical trial unit, FFCD data centres
Several LNC members are involved in key management positions (Dean of Health Faculty, Director of graduate school, deputy director of LipSTIC LabEx, Director of TRANSLAD FHU, Director of Clinical Investigation Center, Director of early clinical trial unit, deputy director of FFCD data centre, Heads of clinical departments, …).
Over the years, three start-ups have emerged from the research works of the unit (Nanodiag, EktaH and Endoquant). The unit conducts state-of-the-art research in different fields of investigations encompassing cancer research, immunology, nutrition and genetic of human diseases. It significantly contributed to health and societal challenges by setting up clinical trials, exploring new therapeutic avenues and developing epidemiologic studies as well as health policy recommendations in various domains. The unit is also strongly engaged in interactions with non-academic players (small/big pharma).

Weaknesses and risks linked to the context

There are no unique subject or strong scientific convergences to gather all the teams except for the translational aspect of their research. In addition, several teams conduct two or more axes of research headed by different PIs and the synergies within the team are not always very clear.
The eight teams constitutive of LNC are dispatched over five different well-apart buildings over the campus. Most teams are split on two or even three sites. The location of all the teams on different sites within the University Campus of Dijon, does not seem to affect teams' cohesion but does not favour direct interactions between distinct groups.
The cohesion of the unit seems very loose: different staff people (students, PARs, Researchers) recognised themselves as members of their respective teams but less as members of the unit.
Whereas lots of publications demonstrated collaborations between the different teams, no interactions or collaborative projects between the different teams are highlighted at the level of the unit.
The prospective scientific policy of the unit is not very well formulated. While the unit does not intend to spread further its scientific diversity, it has not yet clearly identified new technological challenges or strategic fields needing reinforcement. While there was some rotation in team leadership as well as the internal emergence of new group leaders who were sanctioned by the SAB, the unit has not set up a proactive policy to attract new external talents.

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

Strengths and possibilities linked to the context

The unit's human resource management is ensured by a CODIR composed of four persons: the director, deputy director, and two PI. The Unit Council includes all heads of each team, the member of the CODIR, the head of the administrative facility and at least a representative of every other personnel category and meets three times a year. In addition, the team leaders meet regularly to discuss raising matters and appear very satisfied with the new direction.
The unit governance is narrowed and centred, flexible with an organisation of boards for efficiency.
A general assembly is held once a year for general information.
A parity/discrimination referent has been nominated with the objective to comment and influence decision in regards of parity and discrimination.
The referent is involved in a 'gender awareness' program, to educate on the role of the different genders in the workplace by distributing a summary of the FP5 Helsinki report on gender issues and paying particular attention to ensure that extra effort is performed to recruit more women into the project, especially in senior positions or as team leaders.
All the health and safety points are addressed within each team in close collaboration with health and safety (H/S) engineers from INSERM and the University of Bourgogne.

Weaknesses and risks linked to the context

The premature leave of the previous director has not been anticipated. Despite the nomination of a parity referent, the parity could be improved as there is only one female out of four PIs in the CODIR and only three female PI out of nine.
The rules for Health and Safety are respected but a full-time person dedicated to this aspect is missing although a network between the different Health and Safety people of the different teams is in place.
There is no mention of a scientific integrity referent or a sustainable development referent. Actions to reduce the carbon footprint have not been implemented yet.
In addition, how members of the units can report or complain about psychological or sexual harassment, physical or verbal abuse within the unit does not satisfy the students despite the recent identification of a psychosocial risk referent.
The level of communication between the different categories of personals is not optimal and the members of some teams seem to scarcely interact with other teams.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The attractiveness of the LNC centre ranged from very good to excellent.
The unit's members have been highly successful in obtaining funds with a majority of territorial and national origin, although the success in European calls and participation in international consortia could be improved.
While some LNC members contributed to international congresses, the international recognition of more junior members still needs to be improved. No new team has joined the centre.
The involvement in research, training and teaching is excellent with the creation of an international master-doctorate program entitled INTHERAPI.

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

Strengths and possibilities linked to the context

The international reputation of the unit is attested by the participation of several team leaders and PI to scientific journal editorial committees (Cancer Research, Cancers, Dermatology, IJMS, several Frontiers journals, Nutrients, Oncogene, Oncotargets…) or as guest editors. The PI is also well represented in international conferences, with regular oral presentations or invitations (American/European Society for Haematology, American/European Respiratory Society, EMBO/Keystone & CSSL conferences…). Members of the unit also contributed to the organisation of more than 40 conferences and congresses, although essentially at the national level.
The implication of the unit in various learned societies is strong, notably in the fields of oncology, haematology, respiratory research, cell stress, allergies, nutrition, diabetes, toxicology, dermatology, or human genetics. Some PI is implicated in national research evaluation bodies (Inserm CSS2, CSS3, ITMO Genetics, ANSM, France Genomique…).
The success in European calls is still low but one ERC starting grant was obtained (but the PI left the centre) and some teams are members in international contracts including Europeans ones (ERA-NET TRANSCAN2, H2020 Solve-RD, H2020 CBIG-SCREEN, EJP RARE-ILD, MSCA RISE Discover programs). Also, one ERS/EMBO and one EU MSCA postdoctoral fellowships were obtained.
The involvement in research training and teaching are excellent with 77 members having an HDR within 21 defended since 2016. About 80 PhD were defended between 2016 and 2021 (out of a total of 143) but few postdoctoral fellows (27) have been hosted.
The centre has created an international doctoral school (master-doctorate program entitled INTHERAPI for 'Innovative Therapies, Pharmaco-Imaging and Multimodal-Imaging of the University of Burgundy-Franche-Comté) which could improve its attractiveness.

Weaknesses and risks linked to the context

The LNC has not really demonstrated its capacity to attract new teams coming from outside except for one Hospital Professor (from Grenoble) who took over the direction of Team 2, and the arrival of an Inserm researcher from Paris. An international call is planned. Similarly, few non-French people have joined the centre either as PhD students, postdocs, or more senior researchers.

While some LNC members received a good number of invitations to contribute to international congresses, the international recognition of more junior members still needs to be improved.

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

Strengths and possibilities linked to the context

During the last period, the unit has recruited three CRCN, one DR and two technicians/engineers with permanent Inserm positions as well as twelve associated professors, four professors and fifteen technicians/engineers with University or Hospital-associated positions. This important recruitment through the support of INSERM, University and hospital is a good marker of attractiveness. Overall, the support staff appear very satisfied of their hierarchy.
Around 80 PhD students defended their PhD thesis between 2016 and 2021.

Weaknesses and risks linked to the context

Very few non-French people have joined the centre either as PhD students, postdocs, or more senior researchers. The lack of visibility induced difficulties in the recruitment of new leaders coming from external countries and top-level postdoc fellows.
While one PI obtained an ERC starting grant in 2015 to establish his own team, he chose to leave the Institute.
Two new teams were proposed for the next contract; they correspond to individualisation/budding from two large teams. These new PI was selected after evaluation by the SAB. The use of open calls to attract new blood from outside has not been organised during the last period but is planned during the next one.

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

Globally the level of external funding is excellent, and most teams have been very successful in obtaining competitive funding. Notably, the unit is involved in structure and projects funded by the PIA. The Labex LipSTIC (475k€/year) created in 2012 gathers all the teams of the unit and create a certain sense of unity around lipoprotein-related projects. Five teams of the unit (F. Ghiringhelli, L. Apetoh, F. Vegran, C. Thauvin and C. Garrido) also benefited from strong support from the ISITE Bourgogne Franche-Comté (2015–2021, but not renewed).
At the international level, the unit benefited from important investments through FEDER and a few teams were involved in major European projects (ERA-NET-Transcan, EJP-RARE ILD, MSCA Rise, MSCA Respire three, H2020 CBIG-SCREEN, H2020 Solve-RD).
At the national level, the teams of the unit obtained seventeen ANR (10 as coordinator) and seventeen INCa (10 as coordinator). They also obtained strong support through PHRC programs (8 national, 6 inter-regional) and a few grants from other health-related agencies. A very strong support was obtained through the Region Bourgogne Franche-Comté. Finally, they gathered many grants from charities (notably 11 from the Fondation ARC and 38 from the Ligue Contre le Cancer).

Weaknesses and risks linked to the context

Some excellent teams could succeed in securing more European or international funds.
No program to fund a doctorate or post doctorate contracts or engineer and technicians have been organised at the scale of the unit. In particular, the possibility to finance the 4th year of PhD student is still problematic.
The end of the ISITE project will be detrimental to the unit.

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

Strengths and possibilities linked to the context

A major force of the unit relies on the quality of the technologies and core facilities proposed to the teams. The unit has made great efforts to mutualise and develop its technological know-how by creating nine platforms, which will be regrouped in a UMS called BIOSAND at the disposal of the members of the unit.
The platforms were created in coherence with the scientific objectives of the unit and for the development of translational projects to the clinic. These different platforms are in connection with industrial partners which

contracts help to recruit non-permanent staff. 30 out of the 39 technicians and engineers are dedicated to the platform for 50% of their time.
The creation of the UMS is an opportunity to increase the visibility and improve the management and rationalisations of the different platforms.

Weaknesses and risks linked to the context

There is no clear distinction between platforms and 'technical plateau', although all presented platforms seem to be financially balanced.
The creation of the UMS is an opportunity but could also be a threat for the PARs dedicated to it and their adhesion to the project should be secured.
The membership of platforms to their respective academic or hospital structure must be clearly specified.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The unit produced excellent research publications in terms of both number and level of publication. The respective contribution of the individual team is heterogenous, but all of them obtained valuable results. Most of the research articles were published in very well-established journals and 96 out of the 692 PDC publications are within the top 10% of citations, reflecting the high quality and originality of the unit's production.

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

Strengths and possibilities linked to the context

Overall, the unit members published 2007 scientific papers (original publications) between 2016 and 2021, including 692 publications signed as PDC. Most of those publications have a very good international visibility and 96 PDC publications are within the top 10% of citations, which is clearly remarkable. These include several publications in generalist and/or top range speciality journals such as American Journal of Human Genetics, Blood, Diabetes, Gut, Journal of Clinical Investigation, Nature communication, Nature genetics, New England Journal of Medicine, Science Translational Medicine…
20% of the publications are in Oncology, 13% in Genetics & Heredity and 8% Critical Care Medicine, the rest are in biochemistry and molecular biology, haematology, surgery, endocrinology, gastroenterology reflecting the large domain covered by the unit. The production also reflects an excellent continuum of high-quality results from basic to be applied or clinical research, which stands out as a particularly strong feature of the unit.
Of note, fifteen members of the LNC unit are present in the Stanford's List of World's Top-Cited Scientists, i.e. Top 2% Scientists ranking. In addition, many senior members of the unit obtained scientific awards (mostly at national or regional levels), and several young investigators received the best communication awards in conferences.

Weaknesses and risks linked to the context

The level of publication is not uniform among the teams (normalised to the number of personnel).

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

A very significant number of publications have been obtained, with more than a half-being peer-reviewed research papers.
There is an important number of shared publications among teams.
The different staff categories are associated with the production of the unit and all the teams have been productive albeit with differences in volume and level of production.
The unit represents the main force of the University of Bourgogne in the biology-health-science area, contributing to more than 20% of its publications and reaching top-level journals.

Weaknesses and risks linked to the context

Generally speaking, the scientific production is proportionate to the research potential of the unit. Several teams seem to have only one or two publications with another team of the unit and the scientific production of a few teams could be improved.
The unit has not defined general rules concerning the association or acknowledgment of platform support staff in the publications.

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 different team members claim that they are following practices that characterise responsible research conduct. Data generated and published by the UMR respect the open science principal as requested by the recommendation of editorial board on journals. A dedicated storage server is allocated to the UMR1231 at the university Data Center and at both hospitals to allow the traceability, storage, and accessibility of research data.
The ethical principles underlying patients research follow Helsinki declaration. Within publications, contributions seem to be properly considered (particularly in the case of co-signatures) as the comity did not receive complains concerning authorship except from the platform support staff.
PhD students are following courses on research integrity and FAIR data within their doctoral school program.

Weaknesses and risks linked to the context

Most information provided to the comity before and during the visit are clichés and general considerations on scientific integrity, Open science, or DORA recommendations. The unit does not seem to develop strong or specific actions along these lines. Open access represented only 50% of the published articles for which the information was made available to the committee; this percentage dropped to 40% for publications as main authors. No integrity referent or committee has been nominated within the unit. The electronic notebooks are not totally available which could impair a complete traceability.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

Overall, the inclusion of the unit's research in society is excellent. The link between basic research and clinical applications is particularly well established in most teams. Some teams have strong and fruitful interactions with industrial and pharma companies. Others have produced numerous patents and allow the creation of a start-up. Some teams are clearly dedicated to communicating the products of their research to the public.

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

Strengths and possibilities linked to the context

The unit is essentially involved in research relevant to human health and has a very strong record of non-academic interactions. Most actions are performed at the team level, but the general output of socio-economic interactions is impressive.
Overall, there is an excellent continuum between basic and clinical research. Remarkably, unit members are implicated in more than 40 clinical trials, some of which directly stem from their research program. Because of the interconnection between teams and hospitals, most teams were also investigators in industry-driven trials.
The unit established or contributed to important patient cohorts and databases on various diseases (haematological malignancies, digestive cancers, endocrine tumours, inflammatory diseases…). It produced bioinformatic pipelines for genomic analyses of human pathologies and participated in decision-making policies and expertise for health issues management, notably in the fields of diabetes, digestive cancers, toxicology/alimentation, and genetic diseases.
The links with industrial/pharma companies are also remarkable and most teams have contracts with small or big pharma companies (Servier, Roche, Boiron, AstraZeneca, Sanofi, NovoNordisk, Pfizer, Enterome, Gladerma…) for a total of 2.6M€ over six years. A Labcom with Covalab is starting in 2022. Parts of the salaries

of engineers, technicians, or bioinformaticians have been granted by industrial contract. CIFRE PhD fellowships were obtained by four teams (2, 3, 5 and 8).

Weaknesses and risks linked to the context

While each team performs very well, there does not seem to be any systematic unit-level-organized approach to sustain the valorisation effort and to communicate towards potential industrial partners.

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

Strengths and possibilities linked to the context

The unit developed several products for the socio-economic world and interact with SATT SAYENS and 'INSERM-Transfert' when valorisation is needed. It deposited 23 patents, five inventions, one software as well as nine open source software. Four start-up companies were created as spin-offs from research teams (Nanodiag, Orphanomix and Endoquant in the previous mandate; Ektah in 2021). Income from Endoquant (around 200k€ for the evaluated period) was reinjected in the development of the lipidomic analytical facility. Team GAD and NUTOX developed start-ups (Ektah and OrphanOmiX) with the SATT SAYENS
Several unit members have been involved in the production of recommendations from the ANSES, the HAS or other national health authorities and international societies.

Weaknesses and risks linked to the context

There is no dedicated person within the unit to identify, within the work of the different teams, the potential economic, social or cultural impact especially for the teams that are not familiar with those aspects. Still the collaborations with the SATT or Inserm Transfert are very efficient.

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

Strengths and possibilities linked to the context

Several team members participated to or coordinated events for the public (Mars Bleu, Festival de l'alimentation-Cité des sciences et de l'industrie, La Villettes Paris…). The unit is involved in outreach activities, for instance the 'Experimentarium program' organised by the University of Burgundy. Several unit members have strong interactions with the public and take an important part in debates in society, notably around ethical issues on genomics medicine or debates on nutrition, obesity, cancer, and other diseases. Several teams were solicited for media intervention (TV, radio, and national/local newspapers, such as Arte, France Culture, France 3 Bourgogne, Sciences et Vie…).

Weaknesses and risks linked to the context

While some teams perform very well, there does not seem to be any systematic unit-level-organized approach to communicate towards the public, share knowledge and take part in debates in society.

C – RECOMMENDATIONS TO THE UNIT

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

The unit is encouraged to develop a better communication strategy towards the external world (website, international calls, international meetings) but also within the unit itself, to gather all the staff and create a feeling of belonging to the unit and not only to the different teams.
The identity of the unit and of the teams could be improved, with a clearer focus on a common scientific goal for some of them.

Recommendations regarding the Evaluation Area 2: Attractiveness

The unit is encouraged to present an international call to welcome new teams that are not budding from already established teams.
Since some internationally recognised researchers are close to retirement, the unit could develop a program to encourage more junior (and female) researchers to take the lead and increase their international visibility.

Recommendations regarding Evaluation Area 3: Scientific Production

Overall, the publication level of the unit is excellent, but some teams are encouraged to publish in more general journals and not only in the top journals of their speciality.
An effort should be made to follow DORA recommendations in terms of publication, in particular towards open access publication and FAIR data.

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

Some of the teams are excellent in the contribution towards the society. Based on their expertise, the unit is encouraged to develop a strategy to generalise this contribution.

TEAM-BY-TEAM ASSESSMENT

Team 1: CADIR – Cancer and adaptive immune response

Name of the supervisor: Mr. François GHIRINGHELLI

THEMES OF THE TEAM

The CADIR team aims at deciphering the anti-tumour immune response and escape mechanisms in both human and mice with a particular interest on adaptive immune response players with the final goal to identify prognostic and/or predictive markers and develop new combinations of anticancer therapies.
Team projects particularly focus on the role of:

i) CD4 T cell immune response,
ii) chemotherapy and inflammatory cytokines on CD8 immune response,
iii) innate lymphoid cells on the generation of adaptive anti-tumour immune response
iv) and IL1 and NLRP3 in antitumoral immunity.

They also investigate the interconnection between lipid metabolism and tumour immune response and develop a program based on the Artificial intelligence, Bioinformatics and NGS strategy to find new biomarkers.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The recommendations of the previous evaluation were to continue further in excellence by notably writing independently a few strategic review articles for example in Nature Reviews series (NRI, NRC, NRMCB, NRDD) journals that would further increase the international visibility of the team.
In terms of grants and publications, the team is impressive specially the team's leader. Over the period, the team published several reviews in Cancers, Cells and OncoImmunology journals. The team responded to the recommendations.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	10
Lecturer and associate lecturer	5
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)	6
Research supporting personnel (PAR)	9
Subtotal permanent personnel in active employment	**31**
Non-permanent teacher researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	7
Post-docs	1
PhD Students	10
Subtotal non-permanent personnel	**18**
Total	**49**

EVALUATION

Overall assessment of the team

The global scientific output of the team is outstanding. The team contributes at high levels to the development of basic, translational, and clinical analyses in the field of onco-immunology. The team has an outstanding scientific production in highly cited papers. The attractiveness of this team is outstanding with the arrival of several new members. The team was successful in grant funding (international and EU levels) and was remarkably active in establishing collaborations.
In terms of valorisation, the team is outstanding with its involvement in several clinical trials based on its own research and with the deposit of patents.

Strengths and possibilities linked to the context

This is a large research team headed by a PU-PH in oncology and composed of professors, clinicians, scientists, technicians, postdocs, and PhD students.
The team is very well recognised in the field of tumour immunology in France and internationally leading to the high attractiveness for postdocs and fruitful collaborations with renowned teams (Laurence Zitvogel's team, Guido Kroemer's team, Eric Tartour's team, etc.). They recently recruited a bioinformatician to develop the deep learning theme.
The team provided important contributions to the field of Immuno-oncology by the breakthrough discoveries in the domain of anti-tumoral therapies and immune mechanisms such as the discovery of predictive markers of chemotherapy treatments in CRC.
The number of publications (2016–2021) is impressive: more than one hundred original articles. Among the articles published where at least one member of the team signed as principal authors, several are in large audiences (Nat Immunol, two Nat Commun, two JITC, Gut, Cancer Immunol Research) and/or have been highly cited.
The team is highly involved in clinical research through its involvement in clinical trials and has built a real continuum from basic to translational research in the field of immuno-oncology. In terms of valorisation, the team deposited two patents and has developed software in open source. While no spin-off has emerged, this was a deliberate choice of the team to ensure that biomarkers were directly applicable to patients (AI software is on open source).
During the last contract, eleven students have defended their PhD and five postdocs were recruited.
Due to the presence of several PU-PHs and MCU, the team is deeply involved in many formations of the University of Burgundy going from the first university cycle of teaching to Master 2. The team co-shares the responsibility of the organisation of a Master 1 teaching session.
The capacity of the team to fund its research projects is impressive. The financial supports come from national (2INCa, 2 ITMO Cancer as PI) and 3ANR as partner; and international (FEDER, TRANSCAN, 4 contracts with two as coordinator; partner in Quatar foundation) organisations and charities (4ARC, 20 from regional Ligue contre le cancer and 23 from the Region). The team has also obtained seventeen contracts from pharmaceutical companies (Genentech, BMS, Servier...). For more than half of grants or contracts, the team is PI or coordinator.
Over the period 2016–2021, a member of the team obtained an ERC starting grant and to develop his own team.
The PI and the other members of the team are often invited in national and international congress (ESMO, ASCO, FOCIS 2021, WCLC), and participated in the organisation of meetings (ESMO, Canceropole Grand-Est congress).
The PI and members of the team are also involved in the expertise committee for grants (FNRS, PHRC Cancer, ARC, Cancéropole Grand-Est) and for scientific institutions (HCERES).
Members of the team are involved in editorial activities for several journals (Cancer research, Plos One, Cancers).

Weaknesses and risks linked to the context

Given the size and financial resources of the team, the number of postdocs could be more important.

RECOMMENDATIONS TO THE TEAM

The team should finalise a publication of the MEDITREME study, which was presented in congress two years ago. Also, what is expected as regards to translational work would be interesting to present.
The team should put in place a strategy to attract scientific postdocs eligible for CRCN recruitment, that should be easy, given the excellent research and the renown of the team.
We encourage the team to continue the research at this excellent level particularly by favouring as it is already done the development of projects from basic to clinic research.

Team 2: Epi2THM – Epigenetics, Epidemiology and personalised treatments in haematological malignancies

Name of the supervisor: Mrs. Mary CALLANAN

THEMES OF THE TEAM

The team is a relatively new entity which merges the groups of M. Callanan (who joined the unit in 2018) and L. Delva, as well as several clinicians involved mostly in epidemiologic and patient follow-up studies. It develops a research program in basic and translational onco-haematology, aiming to identify and model disease mechanisms, in combination with research that aims at improving diagnostic and treatment of haematological malignancies. The team focuses on epigenetic-related mechanisms, but also develops personalised medicine approaches through the study of minimal residual disease (MRD).

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous report concerns only the SAPHIHR team, which was headed by L. Delva. This group is only one of the components of the presently evaluated team. We note that the current focus of this group (PRMT2 in myeloid leukaemias) is distinct from the projects presented during the previous evaluation. Recommendations were mainly to strengthen the links with the clinic. This has been achieved through the configuration of the new team, which has a large clinical component, and places a strong focus on translational research.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	3
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	2
Research supporting personnel (PAR)	15
Subtotal permanent personnel in active employment	**23**
Non-permanent teacher researchers, researchers and associates	1
Non-permanent research supporting personnel (PAR)	2
Post-docs	1
PhD Students	7
Subtotal non-permanent personnel	**11**
Total	**34**

EVALUATION

Overall assessment of the team

The global scientific output of the team is very good. It has shown a very good to excellent productivity which emanates from all its components. However, while epigenetics is the underlying focus of most of the team, it still gives the impression of being mostly a patchwork of several subgroups which follow separate research interests, with little synergy between them. The team's attractiveness is very good, as it has strengthened its workforce through the recruitment of several staff researchers and engineers and has shown a good ability to secure funding. The team has very good socio-economic interactions thanks to its clinical and epidemiological activities.

Strengths and possibilities linked to the context

The team attempts to build a strong bridge linking fundamental research and clinical research and has merged with several pre-existing entities from both the basic research and the clinical research sides. It thus has a very nice potential to identify novel mechanisms of disease (mostly related to epigenetics) and derive clinical applications from its findings. It has brought together scientists with a strong background in fundamental haematology and clinicians working in the fields of onco-haematology and epidemiology. It has also reinforced its scientific potential through the recruitment of a CRCN with strong experience in genomics and epigenetics and the future recruitment of a probable PU-PH with strong experience in Ct DNA detection. The team has also reinforced its potential through the recruitment of a bioinformatician and the setting up a technical platform dedicated to CRISPR/Cas9 genome editing.
The team has a very good to excellent levels of production with 39 research articles including sixteen as lead authors in highly cited journals (Blood, Leukaemia, Nature Commun, Sci Rep…). Team members have also contributed to several publications as collaborators.
The team is very active in clinical research, as it is leading several clinical trials and is part of several large national networks in the field of leukaemia/lymphoma. It produced a very high number of clinical publications (>200), including a few important ones as lead authors (Am J. Hematol, Lancet Oncol…).
The team obtained four national grants as coordinator (PHRC, ANRS, 2INCa), four from the Region (2 FEDER, CHU Bourgogne, Region Bourgogne) and one from PFIZER.
The team plays an important role in the organisation of the unit, as one of its members is involved in coordinating all of its technological facilities. It is also very well integrated in national networks for haematological cancer research.
Although the team is not directly involved in the valorisation, its links with implication in clinical and epidemiological research has direct socio-economic impact in terms of health management, in particular for blood cell cancers, and the team has developed some outreach activities.

Weaknesses and risks linked to the context

The team appears to be a rather heterogeneous group of people who conduct mostly parallel research projects. There is little convergence between the three main topics (epigenetics, epidemiology and MRD studies). This gives the appearance of scientific fragmentation, with relatively little synergy between the various components, and suboptimal research potential affected to individual projects. This is particularly notable for studies on breast cancer, which are remote from the leukaemia/lymphoma axis. Better integration might, however, be in the workings, as we note the contribution of multiple components of the team to a recent paper (CSH Mol Case Studies 2021). The proposed study of the epigenetic impact of pesticide exposure may bring an interesting fundamental extension to the team's study of epidemiological aspects of pesticide exposure. However, this new project yet adds another topic to the scientific portfolio of the team and seems to dilute rather than strengthen its focus.
The SAPHIHR branch of the team has lost a CRCN who was a major driving force in the projects of this group (last author on all the publications emanating from this subgroup). Some very interesting research projects (link between obesity/high fat diet and leukaemia) have also been stopped because of his departure. The current research topic of this subgroup (PRMT2 and inflammation in the tumour microenvironment), while seemingly having led to interesting results, has not yet led to any publication. It is difficult to judge the strength/potential of this project, which benefits only from limited funding.
While funding has been adequate for the past contract, with strong support for clinical and epidemiological projects at the national/regional level (PHRC, ANRS, FEDER...), the team has relatively little visibility for its funding for the coming years, in particular with respect to its non-clinical projects (only a 50 k€ grant extends beyond 2022).
Visibility of the team in international scientific conferences is relatively limited.

RECOMMENDATIONS TO THE TEAM

The team should try to rethink its scientific strategy to concentrate its forces on fewer projects, with a narrower focus, especially within its fundamental/epigenetic projects, and to tighten the links between its fundamental, epidemiological, and clinical axis of research. Epigenetics of lymphoma seems to be currently the strongest aspects of the team's work and might be privileged. This would help the team build its identity and bolster its visibility at the international level. Allocating sufficient resources to fewer projects may help the team's prospects in securing funding from national grants such as ANR or INCa PLBio, by increasing the quality of its preliminary results as well as the credibility of its work plan.

Team 3: HSP-PATHIES — Heats shock proteins in human pathologies

Name of the supervisor: Mrs. Carmen GARRIDO

THEMES OF THE TEAM

The team studies the role of Heat Shock Proteins (HSPs) in different human pathologies in which a dysregulation in their expression/function is involved, such as cancer, fibrosis, myeloproliferative syndromes, or immune disorders.
After showing the involvement of HSP 27 and 70 in cancer cell survival and the involved mechanisms, the team is currently interested in the role of several HSPs in differentiation, the physiopathological functions of extracellular HSPs, and the possibility to target HSPs in cancer therapies and as a biomarker for cancer diagnosis.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The recommendations were to continue further in excellence, aiming at one highest impact journal papers a year, to consolidate excellence by applying for an ERC grant and to write a few strategic review articles in Nature Reviews series journals (NRI, NRC, NRMCB, NRDD).
The team was encouraged to think about the most optimal structure to accommodate its rapid expansion of recent years, which may involve budding off of new groups.
The number of publications of the team in large audience journals during the past contract demonstrates the excellence of the team. The team did not get an ERC grant, but it is the coordinator for three European contracts (2 FEDER, H2020).
One team member left the team to start an independent team at the LNC. The team was, however, reinforced by four researchers (including one who benefits from an Avenir contract) and two engineers.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	6
Lecturer and associate lecturer	5
Senior scientist (Directeur de recherche, DR) and associate	2
Scientist (Chargé de recherche, CR) and associate	5
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	1
Research supporting personnel (PAR)	5
Subtotal permanent personnel in active employment	**24**
Non-permanent teacher researchers, researchers and associates	4
Non-permanent research supporting personnel (PAR)	8
Post-docs	4
PhD Students	22
Subtotal non-permanent personnel	**38**
Total	**62**

EVALUATION

Overall assessment of the team

This is an outstanding team which produces highly relevant work related to the fundamental and pathological roles of HSPs. The team has a high international visibility with an excellent to outstanding levels of production. It contributed to>300 publications during the contract period, including Nat Com; Blood; Cell Death & Diff. The team has a strong translational activity and obtained numerous results with high clinical potential. The team is well structured into several subgroups led by senior researchers, each of which has an excellent visibility and a remarkable capacity to obtain funding. The attractiveness of the team is outstanding which is concretised by the recruitment of several researchers, MCU, engineers and technicians and one ATIP-Avenir. In terms of valorisation, the team is outstanding with the creation of a start-up as a spin-off based on the team results and more than ten patents.

Strengths and possibilities linked to the context

This is a large team composed of scientists and teaching researchers (16), engineers and technicians (6), postdocs (6) and PhD students (19).
The team has an excellent international recognition in the field of heat shock proteins (HSP), leading to the high attractiveness for postdocs and many fruitful collaborations with local, national and international teams.
The team provided important contributions to the field of HSP through the breakthroughs in the domain of circulating-HSP exosomes and their role in the follow-up of cancer patients.
The attractiveness of the team is excellent and is highlighted by the arrival of two INSERM researchers and the recruitment with permanent positions of one researcher, two MCU-PH, two engineers, the return of a postdoc with an ATIP-Avenir contract.
The output is remarkable in terms of number and quality of publications during the current contract (2016–2021). Team members have contributed to 303 articles in international, peer-reviewed journals, including 112 were issued from research activities of the team (with team members listed as first and/or last/corresponding authors). More than 70 articles correspond to translational/clinical work: Science Transl Med, 2 Nat Commun, 2 Blood, 2 JEV, Death & Diff and several have been highly cited. In addition, the team has obtained>10 patents, of which two have been bought by biotech companies.
During the last contract, 22 students have defended their PhD. The team is involved in a PhD program with Spain and hosts an average of 4–6 international postdocs/year financed by national and European grants (ANR, INCA, Marie Curie fellowship).
The team is involved in education through the presence of several PU-PHs and MCU.
The capacity of the team to fund its research projects is impressive, as all projects are well funded from both national (INCa, 5ANR) and international (4 European contracts, as 2 FederH2020, COFECubBresil, …) Organisations, as well as charities (3ARC, 4Ligue contre le cancer and three labelling LNCC). The team has also obtained contracts from private companies (Inventiva, Sanofi, AstraZeneca, Ipsogen…). For the most grants or contracts, the team is PI or coordinator.
The excellence of the leader and several researchers of the team has also been rewarded by several prizes (Matwin award, prix Avenir Ruban Rose 2016, Fondation Silab Jean Paufique 2018, Odysséa 2017, prix senior Ligue contre le Cancer 2021 and Grand prix de Recherche Ruban Rose 2021).
The PI and the other members of the team are often invited in national and international congresses (ASCO, ECDO, EMBO workshops).
The team has also been active in organising several congresses and meetings (26th Wilhelm Bernhard Workshop on the Cell Nucleus. Dijon; European Respiratory Society task force « Optimising experimental research in respiratory diseases », Journée de Recherche en Allergologie).
Members of the team have also been involved in the expertise committees and scientific committees (AACR, European Cell Death Organization, European project COST).
They are involved in editorial activities for several journals (Oncogene, Oncotarget, Cell Stress & chaperones, The International Journal of Biochemistry & Cell Biology, Frontiers in Oncology and Frontiers in Immunology).

Weaknesses and risks linked to the context

Even though the project of the team is focused on the role of the HSP protein family, this has nevertheless led the team into a very diverse set of research topics, ranging from DNA repair to innate immunity and the biology of extracellular vesicles, as well as a variety of pathologies. The large diversity of the scientific questions may make it difficult to be at the vanguard in each of these fields and fosters relatively little synergy between the individual subgroups within the team. While this diversity might be perceived as weakness, the team has, however, managed to navigate this diversity successfully, by affecting a critical mass of people supervised by a dedicated researcher to each project, and through a strong network of collaborations.

RECOMMENDATIONS TO THE TEAM

It would be important to think about a strategy for the succession of the PI.
Considering the excellent positioning of the team in its field, the review panel strongly encourages the team to apply for ERC grants or another international equivalent.

Team 4: EPICAD – Epidemiology and clinical research in digestive oncology

Name of the supervisor: Mr. Come LEPAGE

THEMES OF THE TEAM

The team focuses on epidemiological studies about gastrointestinal cancers. This research relies on population-based registries. The team is also deeply involved in clinical research; it hosts the clinical research structures of a major cooperative group in digestive cancers (FFCD).

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The recommendation of the previous report was: 'The committee encourages the group to make a plan about how to appropriately arrange the succession of senior researchers (succession planning).'
This point is not directly addressed in the DAE. However, we do see that the team leader is involved in many national and international collaborations, showing that he was able to pursue visibility of the team, having achieved successful succession from previous leaders. Additional researchers were also recruited.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	3
Lecturer and associate lecturer	4
Senior scientist (Directeur de recherche, DR) and associate	2
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)	27
Subtotal permanent personnel in active employment	**37**
Non-permanent teacher researchers, researchers and associates	4
Non-permanent research supporting personnel (PAR)	6
Post-docs	0
PhD Students	5
Subtotal non-permanent personnel	**15**
Total	**52**

EVALUATION

Overall assessment of the team

The team develops research in two directions: clinical research and epidemiological research, both focusing on gastrointestinal cancer. This part is the specific research area of the team. Overall, the evaluation of the team is very good.
The level of publication seems very good (excellent in terms of participation to clinical trials and good in terms of epidemiological research), the attractiveness of the team is good to very good (some new recruitment, but low number of students), the valorisation very good (due to its hosting of the operational unit of the FFCD).

Strengths and possibilities linked to the context

The EPICAD team is headed by a PUPH in hepato-gastroenterology and is constituted of 37 permanent members. During the last contract, the team recruited two statisticians (PhD), a surgeon (MD) and clinical pharmacist (PharmD PhD). Also, nine students have defended their PhD and four researchers have obtained the HDR and two postdoc fellows were hosted by the team.
The team has a longstanding expertise in digestive oncology and implemented for several years a large clinic-biological database, which is the foundation of an active epidemiological research.
The team is the host of the operational structure of a strong national cooperative group in digestive oncology (FFCD). Publications (65 papers with a member of the team as first, last, or corresponding author among which Gut 2019 and 179 additional publications) and funding (PHRC-K) related to FFCD are of high levels.
The team has developed international collaboration within epidemiological research (McGill in Montreal, Canada, IRCSS in Milan, Italy).
The team is also actively involved in clinical research, as it is supporting numerous clinical trials.
There is a strong implication of the team leader in the European society of Digestive Oncology (ESDO), being a member of the board and having masterclasses.
The PI and the other members of the team are often invited in national and international congresses. They have been involved in the organisation of eighteen national and five international conferences.
The PI and members of the team are also involved in the expertise and scientific committees (HCERES, PHRCs, INCa, Ligue, ARC…).
The team is involved in education through the presence of four PU-PHs, one MCUPH and one MCF.
The team has access to biobanks linked to clinical research, and developed research based on these biobanks.
Team members have also participated in events for the public and gave interviews in mainstream press.

Weaknesses and risks linked to the context

Many funding/major publications presented relate to the FFCD structure, and not directly to the proper work of the research team. We would recommend a clear differentiation of the publications/grants led by the team and the publications/grants in which the FFCD is involved. Albeit the role of the team in supporting the FFCD is clearly a positive output of the team, developing its own research would also be important and could be clarified.
The scientific output of epidemiological research is sometimes published in journals with high visibility (Gut), but more frequently in less visible journals.
The team has a low number of researchers and students (2 DR but no CR, five PhD but no postdocs), in comparison to the high number of supporting staff and clinical researchers (27 research supporting personnel, 3 Professor, 4 Lecturers). This is again probably due to the role in the support of FFCD, however, developing its own research would require increasing the number of researchers and students.
The team is involved in international collaborations but did not receive European funding as a coordinating group.

RECOMMENDATIONS TO THE TEAM

Increasing the number of researchers devoted to the research team, as opposed to personal dedicated to operational support of the FFCD, might help to increase the proper output of the research team. Moreover, increasing the number of students involved might also help to redirect efforts to pure research activities.
The link between the registry and availability of samples (made possible by the small number of pathology labs in the region) to create a registry-based biobank is a very good opportunity for much future research.

Team 5: LIPNESS – Lipoproteins and lipid transfer in sterile and sceptic inflammation

Name of the supervisor: Mr. David Masson

THEMES OF THE TEAM

The LIPNESS team gathers molecular and cellular biologists, physiologists, and clinicians to study the impact of lipid metabolism on inflammation processes and inflammatory diseases such as atherosclerosis and sepsis. Two major axes are developed:

1- lipoprotein metabolism and endotoxemia with a specific focus on lipid protein transfer, lipopolysaccharides (LPS) and LPS detoxification to prevent inflammation,
2- fatty acid metabolism and inflammation with a specific focus on polyunsaturated fatty acids (PUFA), liver X receptors (LXR) and mitochondria in relation to cardiometabolic diseases, metabolic syndrome, and macrophage activation.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous recommendation was: 'The strong emphasis on translational research is a key asset and deserves praise. Adjustment in publication strategy should be considered raising the chance of publishing in the highest-profile journals and thereby increase the impact of the work.'

In line with this recommendation, the team has continued to consolidate the translational part of its research by integrating four clinicians since 2020 allowing nine news clinical trials to be carried out since that year. The team also started adjusting its publication strategy as shown by the recent publications, as lead authors, in journals with a large audience in the field (NEJM 2018, JCI 2020).

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	6
Lecturer and associate lecturer	6
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	2
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	6
Subtotal permanent personnel in active employment	**21**
Non-permanent teacher researchers, researchers and associates	5
Non-permanent research supporting personnel (PAR)	5
Post-docs	0
PhD Students	8
Subtotal non-permanent personnel	**18**
Total	**39**

EVALUATION

Overall assessment of the team

The LIPNESS team is internationally recognised for its longstanding expertise in the field of lipoproteins, lipid metabolism and inflammation. The team further strengthened its translational research with the arrival of four clinicians. A careful balance between basic and clinical research should be preserved. The scientific quality of the research and the publication output are excellent. The attractiveness is excellent with an excellent capacity of the team to fund its research. The team should intensify EU funding and postdoc recruitment. The valorisation capacity is also excellent. The overall assessment of the team is excellent.

Strengths and possibilities linked to the context

The LIPNESS team was directed by the previous team leader until the end of the year 2017 and has since been led by the present team leader. The team is presently composed of seven clinicians, four research faculty members, three INSERM researchers, six permanent engineers/technicians and eight PhD students. Ten team members have their HDR.
The team has strongly been reinforced by the arrival of a PU-PH in 2020, a MCU-PH (former PhD student with an international mobility) in 2021, an AHU (also a former PhD student) in 2021 and a CCA in 2021. The team now has a real strike force to carry out research ranging from basic research to clinical research. This is underlined by an impressive number of clinical trials (14 including 9 since 2020) to evaluate clinical practices or medical devices related to septic shock and the inflammatory response.
The LIPNESS has strong interactions with other LNC teams (PADYS, CADIR, EPICAD).

The LIPNESS team led to major scientific advances in their field, including the development of new prognostic and therapeutic tools/strategies for management of sepsis. The team published fourteen reviews and 332 original articles: 96 from scientific research (30% as lead authors) and 236 from clinical research (40% as lead authors), mostly in large audience-specialised journals (J Lipid Res, Diabetes, Front Immunol) but also in leading general journals (JCI 2020, Cell Reports 2017 and 2020) and in well-recognised clinical journals (NEJM 2018) with lead positions. Of note, 21% of their publications are in the Top 10 citations, 25% of them with lead positions. Apart a MCU, all tenured researchers/teaching researchers/clinicians are publishing with lead positions. Their national and international collaborations led to publications in reference journals (the Lancet, Nature Immunology, Blood), which demonstrates the recognition of their expertise at high international level.

During the last contract, twelve students have defended their PhD and eight PhDs are ongoing. Only one postdoc has been recruited. Among the twelve defended PhD theses, only one PhD student did not yet publish an article as first author. The team is deeply involved in education through the presence of several PU-PHs and MCU.

The team generated three international patents since 2017 and is involved in the 'EndoQuant' business unit (created in 2013 thanks to a previous patent) dedicated to reliable quantification of endotoxins in biological samples. Several funding were secured from national (3 ANR including 2 as PI, PHRC), regional (iSITE-BFC, Labex LipStic...) and international (1 ANR PIA-FEDER, 1 ANR PRCI, FFCR) grants. Considering only grants obtained as PI, around 350 k€/year were secured over the considered period. The team also has strong interactions with private industries (MERK, Netris Pharma-SATT/Sayens, VALOREX).

Some team members were invited to international meetings (JFN 2018, euro Fed Lipid Congress and Expo 2018). The team has organised national (French Atherosclerosis Society since 2016, AFERO 2020, 13th GERLI 2017) and international (JFN 2021, Annual Congress of the American Nutrition Society 2018) meetings.

Team's members participate in research evaluation at the French (ANR, HCERES) and European (Belgium, Netherlands, Poland) levels. Members also belong to French (French Atherosclerosis Society, AFERO, French nutrition society) and International (European atherosclerosis society) societies with management responsibilities, have editorial responsibilities (BMC anaesthesiology, J. Clin Med, PPAR Research…), and belong to the ANSES. Team members disseminated their research to the general population through various media (press, television, radio, social networks), participated in public social events (fête de la science, nuit des chercheurs) and are promoting science to college and high school students.

Weaknesses and risks linked to the context

Despite its location on three distinct sites, the quality of the scientific exchanges between team members as well as the cross-fertilisation between basic and clinical research is preserved thanks to regular meetings.

The increasing size of the clinical part of the team must not be detrimental to basic research that remains to be a driving force for the translational research and the recruitment of high-level postdocs.

As the iSite-BFC was an important source of funding for the team's projects, its end could represent a risk for the team.

RECOMMENDATIONS TO THE TEAM

During the last period, the research works of the team were impressive with an increasing force in translational research. The team is encouraged to prioritise the projects to avoid scientific dispersion and to maintain its highly and balanced complementary expertise between basic and clinical research, which will allow to continue to publish in high quality journals.
Efforts must be considered increasing international/EU funding and recruit young valuable scientific researchers.

Team 6: PADYS – Pathophysiology of dyslipidaemia

Name of the supervisor: Mr. Bruno VERGES

THEMES OF THE TEAM

The Team PADYS works on the pathophysiology of dyslipidaemia associated with diabetes and insulin-resistance, mostly in humans, according to three axes:

1- Dysfunction of lipid metabolism in diabetes and insulin resistance
2- High-density lipoproteins (HDLs) in diabetes and insulin resistance
3- Involvement of the endocannabinoid system in diabetes and insulin resistance.

This last theme is carried by a CRCN researcher, who joined the team in 2017.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Previous report conclusion:
'Overall, the research performed by the team is ambitious and should lead to innovative results. However, the large number of proposed investigations in vivo (in human and mice) and in vitro may be difficult to realise in the absence of new recruitment, especially full-time permanent researchers, or postdocs. The recruitment of a new highly talented full-term researcher in the close future should solve this issue. There is also a need to increase the coordination or the participation in national and European projects and funding, especially to attract more postdocs.'

The team has globally addressed the recommendations of the previous Hcéres report. They made efforts to seek European and ANR funding. 'Three different leaders of the team are either PI or co-PI of ANR project, notably: the EndoROP project on Endocannabinoid and retinal vascular development in Retinopathy of Prematurity (145 k€) and 'Study of qualitative and functional lipid disorders in patients who were infected by SARS-CoV2 in order to detect potential atherogenic sequels' (368k€).

The recruitment of a single CR1, already effective at the time of the previous evaluation, is a plus for the team, but would need to be complemented by other recruitment or mobility of full-time researchers. The attractiveness of the researchers but also of the postdocs must be further reinforced.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	4
Lecturer and associate lecturer	5
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)	0
Research supporting personnel (PAR)	2
Subtotal permanent personnel in active employment	**12**
Non-permanent teacher researchers, researchers and associates	2
Non-permanent research supporting personnel (PAR)	3
Post-docs	2
PhD Students	1
Subtotal non-permanent personnel	**8**
Total	**20**

EVALUATION

Overall assessment of the team

The team had a very good to excellent scientific production, able to provide both observational and mechanistic studies in vitro, in vivo and in clinical settings. They report modifications of the HDL lipidome in diabetes and obesity. Work on the endocannabinoid system (ECS) shows its deleterious effects in the context of diabetes and metabolic syndrome. The valorisation is excellent: a patent on the inhibition of ECS was filed in 2017 and extended to Canada and USA in 2018. The leader of the team participates in many scientific conferences, expert committees and does scientific popularisation. He ensures a good outreach of the team, with the help of new PU-PH and the researcher who joined their team in 2017. The attractiveness of the team is very good but needs to be further improved. Globally, the Team 6 has very good to excellent evaluation.

Strengths and possibilities linked to the context

The PADYS team has been expanded to include five PU-PH, one professor, three MCU and one clinician and one full-time researcher. It also includes two PhD students, one master 2 student and four technical staff. The involvement of the physicians in the team is very important, they are seven out of the nineteen members of the group. Two postdocs were recruited, and two PhD students defended their thesis during the period, one of them became a lecturer at Université de Bourgogne. Both have published articles in good speciality journals and one has been recruited in this same laboratory. They have currently recruited a Canadian postdoc to add visibility to the team.

The team had a good scientific production during the period: 187 publications in international journals with peer review, including about 100 publications with good visibility in very good speciality journals (Diabetes Care, Cardiovasc. Diabetol., Diabetes, AJP Endocrinol Metab and several Arterioscler. Thromb. Vasc. Biol).
The team leader has a good visibility with>350 publications and is invited in numerous national and international meetings in Morocco, Lebanon, Argentina, etc. Since 2019, another clinician is also invited in different congresses and symposia mainly at the national level. The team participates in the organisation of meetings, being part of several scientific committees of European federation/associations for the study of diabetes. They also demonstrate an important participation in national societies such as SFD, and a good expertise (evaluation of laboratories and research projects).
This team has a good capacity to finance projects at local (SATT Grand Est), national (1 ANR, ANRS, PREPS), as well as projects in collaboration with six pharmas (AstraZeneca, NovoNordisk,..). The external funding capacity of the team is thus excellent, with more than 400k€/year.
Since its creation, the team has developed original translational research, particularly on the study of drugs used in diabetic patients that may have effects on lipid profiles (SGLT2i, GIP/GLP1 receptor agonists). On the other hand, the studies carried out on the lipidic composition and the functionality of HDL in diabetic situation is very original and recognised at the international level. It uses the lipidomics platform and allows collaboration with other teams of the unit. Finally, the arrival of a researcher specialised in the endocannabinoid system allows the development of an original and promising axis on this theme. This line of research has notably allowed the filing of a patent on the use of agents blocking the CB1R, the valorisation of which represents an important opportunity.
The evolution of the team beyond this mandate has also been considered, especially in terms of management, which is a positive point.

Weaknesses and risks linked to the context

There is only one full-time researcher focusing on the endocannabinoid system and its interaction with diabetes and insulin resistance. It is important to reinforce the themes carried out by this researcher within a team whose research objectives are more clinical.
Special attention must be paid to the attractiveness of PhD students (currently only one PhD student for 9 HDR).

The patent on the modulation of the hyperactivation of the endocannabinoid system using therapeutic molecules predates the arrival of the researcher in the unit. A follow-up is encouraged beyond the extension to Canada and the USA (search for a company for the valorisation). The recruitment of a single CRCN, already effective at the time of the previous evaluation, is a plus for the team, but the globally limited number of researchers is a weakness to be addressed.

RECOMMENDATIONS TO THE TEAM

The team is very strong in terms of scientific, clinical, and translational production, as well as in terms of national and international influence. More connections between the three axes would be expected and would allow a certain synergy within the team. The research efforts on mechanisms undertaken must continue. If possible, try to increase the team's activity, to attract full-time researchers (recruitment or transfers) and especially thesis and postdoctoral students who would allow the whole unit to participate even more in scientific and medical research. The recruitment of a single CRCN, already effective at the time of the previous evaluation, is a plus for the team, but would need to be complemented by other recruitments or mobility of full-time researchers. The attractiveness of the researchers but also of the postdocs must be further reinforced. The visibility of young people must also be promoted.

Team 7: NUTOX – Nutritional physiology and toxicology

Name of the supervisor: Mr. Naim KHAN

THEMES OF THE TEAM

NUTOX team explores the implication of oro-intestinal lipid sensing in health and disease and assesses how contaminants of endocrine disruptors interfere with its physiological regulation. This team was a pioneer in this field by demonstrating the existence of the 6th taste modality, devoted to lipid taste perception. By using a combination of approaches based on molecular and cell biology, physiology and eating behaviour in transgenic mice invalidated for key targets of lipids taste perception (CD36, GPR120) and human cohorts, the team developed three complementary axes:

1- Mechanisms of detection/absorption of dietary fat along the oro-intestinal tract
2- Regulation and dysfunction in health and disease, particularly in obesity
3- Applied research to assess the hazard of food contact materials

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous recommendations were: 'Overall, the research performed by the team is ambitious and original and should lead to innovative results. However, the large number of in vivo and in vitro projects may be difficult to realise in the absence of new recruitment, especially full-time permanent researchers but also postdocs. The team should try to get EU funding.' Over the past period, the team successfully completed its ambitious project, and even more, with several major scientific advances in their field. The team also generated new tools (immortalised mouse and human taste bud cell lines; 2 Enveloppes Soleau) used by a newly 2021 founded start-up 'EktaH' (2 patents) and new bioassays and was at the origin of the set-up of two technical facilities (Packtox, Metabolics starting in 2007) offering a strong service to industrials. Opening towards more translational research was also made during the past period, the team being presently involved in a phase 1 clinical trial. In line with the previous recommendations, the team was very successful in recruiting four postdocs during the past period. One MCU researcher, but no full-time researcher, was recruited. Whereas no specific EU funding was obtained, international funds outside Europa (3 Programs Hubert Curien and one grant from the USA; 230k€) and two grants from Spain and Germany (100k€) were secured during the last period.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	5
Lecturer and associate lecturer	5
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	0
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	8
Subtotal permanent personnel in active employment	**18**
Non-permanent teacher researchers, researchers and associates	5
Non-permanent research supporting personnel (PAR)	9
Post-docs	4
PhD Students	5
Subtotal non-permanent personnel	**23**
Total	**41**

EVALUATION

Overall assessment of the team

The scientific output and the academic reputation of NUTOX teams are excellent. The team made several very novel discoveries in the field of lipid sensing, which allowed exploration of potent novel pathophysiological mechanisms at the onset of obesity. The publication output is very good. Team attractiveness is very good to excellent: the capacity for funding is very good but academic national grants such as ANRs are rare; the human resources are excellent, especially for postdocs. The valorisation is excellent to outstanding. The team was a driving force for the creation of a start-up (EktaH) and new bioassays that are very attractive to industries. The team is at a stage where participation and/or coordination of EU grants can be considered. The overall assessment of the team is excellent.

Strengths and possibilities linked to the context

The NUTOX team is directed by the present leader since the retirement of the previous leader at the end of 2018. The team is presently composed of eight research faculty members (5 PU, 3 MCU), one clinician (PU-PH), eight permanent engineers/technicians, four postdocs and five PhD students. Seven team members have their HDR.

The team produced 100 articles (nearly twice more since the past period), 55% of them as lead authors. Most of them were published in large-audience journals of the field (FASEB J, Clin Nutr, J. Nutr Bio, Cell Rep, J Lipid Res…). Whereas only 4% of their publications are in the Top 10 citations, 75% of them are with lead positions. The team leader was also invited to write a review in the prestigious Physiological Review and Progress in Lipid Research. The team has developed several national and international (USA, Belgium, Czech Republic, Japan, Austria, India, Sweden, Germany) collaborations leading to publications in specialised journals (FASEB J, PLOSone, J Neurol Sci, Nutrients Acta Physiolgica…). The team also interacts with other LNC teams. Apart from a PR, all tenured researchers/teaching researchers/clinicians are publishing with lead positions.

The team generated two international patents (EU, USA), deposited two Enveloppes Soleau to protect the intellectual property, and founded in 2021 the start-up 'EktaH', which is dedicated to the synthesis of novel fat taste modulators to design new anti-obesity therapies. Team members are PIs of several regional (2 SATT-SAYENS, 2 BFC, 3 AgroSupDijon), national (PNRPE, FRM) and international (3 Programs Hubert Curien, Cargill USA, Brain Germany, BIOMAR Spain) grants. They were also partners in other national grants (1 ANR, 1 ANSM, 1 PNREST). The total amount secured over the six-year period was 1852 k€.

The team leader has an excellent national and international visibility with several invited conferences to international congresses (Federation of European Physiological Societies 2017 & 2019, International African Congress of Nutrition 2017 & 2018, Syscon Conference 2018, Science and Technology Exchange Program 2019 & 2020, Europhysiology 2018, Physiological Society and Integrative Biology 2019, Federation of Indian Physiological Societies 2019, International Congress on diabetes and nutrition 2021, Tunisian Society of Nutrition 2021…). The team leader received the French 'Prix de l'Académie de Médecine' (2020) and the Iranian 'Mustapha Foundation International Prize'.

The team is attractive. During the last period, NUTOX has been reinforced by the arrival of one PU-PH (Head of the Stomatology Department, Hospital Center) in 2017 who brought expertise in clinical research, particularly for the recruitment of human subjects for immortalising taste bud cell lines. One member was promoted to Professor in 2018, which allowed the recruitment in 2019 of a MCU expert in the field of entero-hormones secretion, which facilitates the transversal interaction between NUTOX and LIPNESS teams. During the last contract, ten students have defended their PhD. Of note, eight PhDs were/are in co-supervision with foreigner countries: Algeria (3), Tunisia (2), Czech Republic (1) and Pakistan (2). The team has recruited five postdocs during that period.

Team members participate to research evaluation at national (PNRPE, FRM, INRAE, HCERES, ANR, CNRS) and international (Belgium, Algeria) levels. One team member is an expert since 2015 at the French agency ANSES and was auditioned in 2019 at the French Parliament on endocrine disruptors and plastics. Team members are very active in the diffusion of their research through local and national (AR Cœur en Action, clubs, forums, Mayor of Dijon…) interactions and with the socio-economic world. The team organise every year the 'Village Goût Nutrition Santé' since 2002.

Several team members have editorial activities (Nutrients, PLoS One, Frontiers in Physiology, Acta Physiologica, Molecules, Journal of Stomalogy, Clinical Investigations in Ageing). The team has organized several national

(Annual congress of the French Physiological Society 2019, GERLI 2017) and international (Indo-European Congress 2019, European symposium 'ECOPA' 2019) meetings.

Weaknesses and risks linked to the context

Even if the team manages its ambitious research program very well so far, no full-time researcher is present in the team.
The time devoted to the development of activities with socio-economic added value has increased sharply during the previous period, which can embolise members to the detriment of basic or clinical research activities.
The team was not involved in European grants and participated only to one ANR during the past period.

RECOMMENDATIONS TO THE TEAM

The NUTOX research works led to several very novel discoveries in the field of lipid sensing. Its impressive input in building a new start-up/facilities/bioassays represents a strong attractiveness for industries. The team must be vigilant to maintain a balance between scientific research and industrial collaborations.
The team must set up a strategy to improve their participation and/or coordination in ANR and EU grants. This would be essential to attract high-level postdocs and to recruit them as full-time scientific researchers.
The team is encouraged to pursue its effort to identify the future team leader to secure the team.

Team 8: GAD – Genetics of developmental abnormalities

Name of the supervisor: Mrs. Christel THAUVIN

THEMES OF THE TEAM

GAD team aims to elucidate the molecular basis of rare developmental diseases, to diminish the diagnostic deadlock and to move to therapeutic trials. The research program includes seven themes (T):
Scientific themes:

- T2: Mosaic developmental disorders: clinical description, discovery of new genes and therapeutic trials.
- T3: Translational genomics (with FHU TRANSLAD): exome/genome sequencing in urgent neonatal and prenatal situations.
- T4: OMICS to limit diagnostic impasses.
- T5: Mouse biology and neurodevelopmental pathologies.

Valorisation, networks, and communication themes:

- T1: Increase in knowledge via data sharing (Solve-RD)
- T6: Orphanomix spin-off (SATT Grand-Est), bioinformatics and interpretation of exome/genome sequencing
- T7: Communication: AnDDI-Rares, European ITHACA network

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

In line with the recommendation of the previous rapport encouraging applying to international grants, GAD team gained visibility at the international level and is currently involved in the European project Solve-RD.

According to the recommendation suggesting narrowing down the scope of its research, GAD team choose to in depth study the Cohen's syndrome and some mosaic dermatological developmental disorders.
To study the pathophysiological mechanisms of Cohen's syndrome, a disorder due to biallelic pathogenic variants in VPS13B, the team relies on functional tests on patients' fibroblasts and on preclinical models.

Among the patients with mosaic dermatological developmental disorders, the patients harbouring a phosphatidylinositol-3-kinase activation have been involved in three therapeutic trials. The benefit-risk assessments were not sufficiently favourable to pursue the use of the treatments of the first two trials. The last trial is in progress.

As suggested by the previous evaluation to develop functional connections with other groups within the LNC teams, the GAD team federated a local bioinformatics platform (GIMI). Due to the specificity of the research of the molecular aetiology of developmental disorders, an important research axis of this team sustained by two themes ('translational genomics' and 'OMICS'), most of the team's connections are established with national and international groups working in the same field.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	9
Lecturer and associate lecturer	2
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)	0
Research supporting personnel (PAR)	36
Subtotal permanent personnel in active employment	**48**
Non-permanent teacher researchers, researchers and associates	4
Non-permanent research supporting personnel (PAR)	9
Post-docs	0
PhD Students	10
Subtotal non-permanent personnel	**23**
Total	**71**

EVALUATION

Overall assessment of the team

GAD team studies the molecular basis of developmental disorders and has an excellent scientific output. The team has established a solid network of scientific collaborations and has a steady capacity to obtain funding. Pioneers in human genomics at national level and highly visible in developmental disorders at European level, the team has an excellent attractiveness. The valorisation and the socio-economic interactions are excellent, and the communication is outstanding. Overall, the evaluation of the team is excellent.

Strengths and possibilities linked to the context

Since its creation in 2011, the GAD team was rapidly reinforced with the arrival of new members (including teaching researchers, engineers, technicians, and students) and is currently consisted of 48 permanent members. During the last contract, the team recruited a researcher specialised in mouse neurobiology who obtained an Inserm position (CRCN) in 2019. The team also recruited an expert in genomics and novel molecular technologies, who obtained a MCU-PH position in 2021, as well as a lecturer in the Faculty of Biology (as part of the NeuroGeMM group) and a medical doctor expert in clinical trials.

The GAD team is involved in many collaborative studies aiming to characterise the molecular basis of developmental disorders. The resulting scientific output is significant. The research conducted by the team has led to advances in the molecular diagnosis and in the pathophysiology of several developmental disorders.

During the period 2016–2021, GAD team published 89 papers with a member of the team as first, last, or corresponding author, among which two Nature Genetics (2018 and 2019) and two American Journal of Human Genetics (2016 and 2018). They are collaborators on more than 200 additional publications.
The team members are often invited in genetics seminars. They have participated in the organisation of six meetings about next generation sequencing in medicine.
During the last contract, three members obtained their HDR, eleven students have defended their PhD and two postdocs were hosted in the team.

The level of funding is excellent, including, as project leader, a financial support from PRME, PREPS, ISITE BFC, PPR-maladies rares, Filière de santé, 6Fondation Maladies rares, 4PHRCi, 10Conseil Régional Bourgogne Franche-Comté, FEDER, 2ANR JCJC, and as partner from the European project Solve-RD.
The group leader is involved in numerous French institutions (ITMO Genetics, Inserm CSS2, France Genomique 2025, HAS) and several team members are implicated in learned societies.
Several team members are involved in the medical care and have access to many patients with developmental disorders, for whom they wish to reduce wandering and diagnostic impasse. This team developed, therefore, a significant effort to implement genomic medicine in clinical practice.
The socio-economic interactions are very strong. In addition to contract with two pharma (Pfizer, Sanofi,) and participation in three clinical trials, the team filed one patent and valued two inventions. It also produced eight bioinformatic analyses pipelines
Team members are involved in the coordination of the national centre of developmental anomalies (AnDDI-Rares) and part of the European research network (ITHACA). They also have close interactions with patient associations and are regularly invited in national and regional media. GAD PhD students and young researchers are involved in the 'Experimentarium program', which is organised by Mission Culture Science of the University of Burgundy in Dijon.

Weaknesses and risks linked to the context

The involvement of several members of the team in numerous networks and committees may be time consuming and be, therefore, a hindrance to the direction of the team's research projects.
The vastness of the field of developmental disorders and the large recruitment of patients with no molecular diagnosis make difficult to focus on well-defined projects.
Synergies between the different team leaders are not clear.
The lack of more fundamental scientists makes difficult the development of ambitious functional studies and the recruitment of high-level postdoctoral researchers.

RECOMMENDATIONS TO THE TEAM

The team is encouraged to transfer recent developments in genomic medicine to the molecular diagnostics laboratory and continue to focus on research of subsets of developmental disorders. For instance, the team is encouraged to study in depth some of the neurodevelopmental genes identified in patients and use cellular or animal models to test new therapeutic issues.
The team is encouraged to make the developed bioinformatics tools available online, for use by the scientific community.
The team is encouraged to widen its recruitment of PhD and postdoc at the international level.

CONDUCT OF THE INTERVIEWS

Date(s)

Start: 09 janvier 2023 à 8 h 30

End : 10 janvier 2023 à 17 h 30

Interview conducted: on-site or online

INTERVIEW SCHEDULE

Programme des entretiens entre l'Unité Lipides, Nutrition et Cancer (LNC) et le Comité d'évaluation Hcéres

Lundi 9 et mardi 10 janvier 2023

9 janvier 2023

8 h 30-8 h 45	Présentation des membres du Comité
8 h 45-9 h 25	Présentation du bilan par le directeur de l'Unité (20 min de présentation, 20 min de questions)
9 h 25-9 h 40	Pause-café
9 h 40-10 h 20	Equipe 1 : Cancer and adaptative immune response (François Ghiringhelli) (15 min de présentation, 15 min de questions)
10 h 20-10 h 50	Equipe 2 : Epigenetics, epidemiology and personalised treatment of haematological malignancies (Mary Callanan) (15 min de présentation, 15 min de questions)
10 h 50-12 h 30	Réunion à huis clos du comité
12 h 30-13 h 30	Pause déjeuner
13 h 30-14 h	Equipe 3 : Heat shock proteins in human pathologies (Carmen Garrido) (15 min de présentation, 15 min de questions)
14h-14h30	Equipe 4 : Epidemiology and clinical research in digestive oncology (Come Lepage) (15 min de présentation, 15 min de questions)
14 h 30-15 h	Equipe 8 : Genetics of developmental abnormalities (Christel Thauvin) (15 min de présentation, 15 min de questions)
15h-15h15	Pause-café
15 h 15-17 h	Réunion à huis clos du comité

10 janvier 2023

9h-9h30	Equipe 5 : Lipoproteins and lipid transfers in sterile and septic inflammation (David Masson) (15 min de présentation, 15 min de questions)
9 h 30-10 h	Equipe 6 : Pathophysiology of dyslipidaemia (Bruno Vergès) (15 min de présentation, 15 min de questions)
10h-10h30	Equipe 7 : Nutritional physiology and toxicology (Naim Kahn) (15 min de présentation, 15 min de questions)
10 h 30-10 h 45	Pause-café
10 h 45-12 h 15	Réunion à huis clos du comité
12 h 15-13 h 30	Pause déjeuner
13 h 30-14 h	Rencontre avec les personnels d'appui à la recherche administratifs et techniques Porte-parole : Nicolas Pernet (Nicolas.Pernet01@u-bourgogne.fr)
14h-14h30	Rencontre avec les doctorants et postdoctorants Porte-parole : Mannon Geindreau (mannon.geindreau@u-bourgogne.fr)
14 h 30-15 h	Rencontre avec les chercheurs et les enseignants-chercheurs Porte-parole : Laurence Dubrez (laurence.dubrez@u-bourgogne.fr)

15h-15h15	Pause-café
15 h 15-15 h 45	Réunion du Comité avec les représentants des tutelles Université de Bourgogne : vp.recherche@u-bourgogne.fr Délégué Inserm : Eric Simon (eric.simon@inserm.fr), IT PMN: Raymond Bazin (raymond.bazin@inserm.fr) et Chantal Boulanger (chantal.boulanger@inserm.fr), IT Cancer: Alain Eychenne (alain.eychene@inserm.fr), IT GGB: Emmanuelle Génin (emmanuelle.genin@inserm.fr) Représentant Agrosup : François Roche-Bruyn (francois.roche-bruyn@agrosupdijon.fr)
15 h 45-16 h	Pause-café
16h-16h30	Réunion à huis clos du Comité
16 h 30-17 h	Réunion du Comité avec le Directeur d'Unité et le Directeur Adjoint
17h-17h30	Réunion à huis clos du Comité

PARTICULAR POINT TO BE MENTIONED

N/A

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UNIVERSITÉ DE BOURGOGNE

Le Président

à

Monsieur Éric Saint Aman
HCERES
Directeur du Département d'évaluation
de la recherche
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75013 Paris

Dossier suivi par :
Colette SCHMITT
Directrice du Pôle Recherche
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Dijon, le 8 juin 2023

Objet : Evaluation HCERES DER-PUR230023278 - LNC - Lipides, Nutrition, Cancer

Monsieur le Directeur,

Je vous remercie pour l'envoi du rapport d'évaluation comportant un avis globalement très positif sur le laboratoire Lipides, Nutrition, Cancer (LNC).

Son Directeur, Monsieur François Ghirhinghelli, souligne la qualité de l'analyse et remercie les membres du comité de visite pour leurs propositions.

Je tiens enfin à réaffirmer le soutien de l'université de Bourgogne à cette unité de recherche.

Je vous prie d'agréer, Monsieur le Directeur, l'expression de toute ma considération.

Vincent THOMAS
Président de l'université de Bourgogne

UNIVERSITÉ DE DIJON
Le Président

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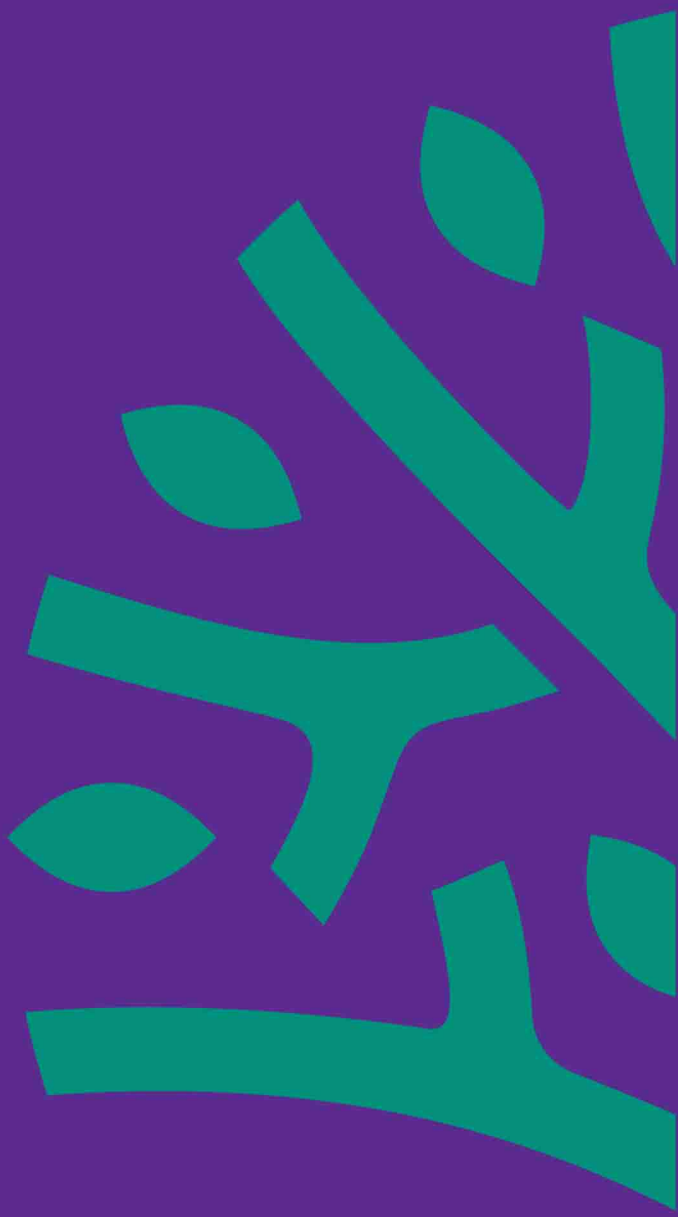

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