

EVALUATION REPORT OF THE UNIT
IRFAC - Interface recherche fondamentale et
appliquée en cancérologie

UNDER THE SUPERVISION OF THE
FOLLOWING ESTABLISHMENTS AND
ORGANISMS:

Université de Strasbourg
Inserm

EVALUATION CAMPAIGN 2022-2023
GROUP C

Rapport publié le 21/08/2023



In the name of the expert committee¹ :

Robert-Alain Toillon, President of the committee

For the Hcéres² :

Thierry Coulhon, President

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

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

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

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

MEMBERS OF THE EXPERT COMMITTEE

Chairperson: Mr Robert-Alain Toillon, Université de Lille, Villeneuve d'Ascq

Experts: Mrs Corinne Bousquet Centre de Recherches en Cancérologie de Toulouse (CRCT) ; CSS2
Mrs Marie Loosveld Centre d'immunologie de Marseille-Luminy (CIML); APHM, Hospital La Timone, Laboratoire d'Hématologie, Marseille; CNU 47-01
Mr Serge Roche, Centre de Recherche de Biologie Cellulaire (CRBC), Montpellier; panel expert
Mr Niclas Setterblad, Sorbonne Paris Cité; PAR

HCÉRES REPRESENTATIVE

Mrs PALLADINO Francesca

CHARACTERISATION OF THE UNIT

- Name: Interface recherche fondamentale et appliquée en cancérologie
- Acronym: IRFAC
- Label and number: UMR-S1113
- Number of teams: 3
- Composition of the executive team: Jean-Noël FREUND

SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement

SVE6 Physiologie et physiopathologie humaine, vieillissement

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

THEMES OF THE UNIT

The general themes focused on the role of transcription factors, essentially tissue – specific, in epithelial cancers, namely CDX1/CDX2 in intestinal cancers (Team 1), p73/p63/p53 in gastric cancers (Team 2), and homoeostasis and cancer (Team 3, created in 2020).

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The UMR-S1113 was created on January 1st, 2013. At the time it comprised three research teams, two of which were renewed in 2017 and were then reinforced by the arrival of a third team in 2020. It is housed in a building owned by Inserm, located close to the University Hospital of Strasbourg-Hautepierre.

RESEARCH ENVIRONMENT OF THE UNIT

The UMR-S1113 is part of the Excellence Initiative (IdEX)' Beyond Frontiers'. Teams 1 and 2 have been largely involved in the creation of the ITI (Institut Thématique Interdisciplinaire, ex-Labex) InnoVec launched in March 2021. Team 1 is also a partner of the regional FHU (Fédération Hospitalière Universitaire) ARRIMAGE. The unit is involved in COST Action Proteocure EU (WP4 co-leader).

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

Permanent personnel in active employment	
Professors and associate professors	14
Lecturer and associate lecturer	7
Senior scientist (Directeur de recherche, DR) and associate	4
Scientist (Chargé de recherche, CR) and associate	7
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	11
Subtotal permanent personnel in active employment	42
Non-permanent teacher-researchers, researchers and associates	15
Non-permanent research supporting personnel (PAR)	4
Post-docs	3
PhD Students	16
Subtotal non-permanent personnel	38
Total	80

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

Employer	EC	C	PAR
Université de Strasbourg	17	0	2
Inserm	0	8	7
Centre Paul Strauss	1	1	2
CHU Strasbourg	3	0	0
CNRS	0	1	0
Total	21	10	11

UNIT BUDGET

Recurrent budget excluding wage bill allocated by parent institutions (total over 6 years)	2,859
Own resources obtained from regional calls for projects (total over 6 years of sums obtained from AAP idex, i-site, CPER, territorial authorities, etc.)	425
Own resources obtained from national calls for projects (total over 6 years of sums obtained on AAP ONR, PIA, ANR, FRM, INCa, etc.)	2,397
Own resources obtained from international call for projects (total over 6 years of sums obtained)	144
Own resources issued from the valorisation, transfer and industrial collaboration (total over 6 years of sums obtained through contracts, patents, service activities, services, etc.).	237
Total in euros (in K €)	6,062

GLOBAL ASSESSMENT

The committee did not meet the unit and the list of questions to the Director was not returned to the experts. This report is based on the documents provided only.

The unit UMR-S1113 (Interface recherche fondamentale et appliquée en cancérologie, IRFAC) comprised three teams. This organisation has led to the development of research that covers broad areas: cancer initiation and progression (Team 1); molecular mechanism of therapy response/resistance to therapies (Team 2); homoeostasis and cancer (Team 3, created in 2020). Research of the unit is based on a multitude of cellular and/or physiopathological models of leukaemia, head and neck cancer, digestive cancers, and investigates various molecular pathways (CDX2, p53, chemokine...). The publications obtained by the unit are excellent, with 44 publications as PI (1 Elife, 1 J Exp Med, 1 Cell Death and Differentiation, 1 Oncogene, 2 Cancer Letters...) and one Nature in collaboration. The unit also produced 164 clinical publications as PI in Am. J. Hematol., Ann. Oncol ..., Cancers, and two in collaboration as one NEJM, 1 Blood... The research of the unit is mainly fundamental, but the integration of clinicians has made it possible to transpose results into the clinic (3 clinical trials, 3 biological collections, FHU Arrimage). The multiplicity of the research topics and model systems used by the different teams and also within the same team (team 2) remains a high risk because of the dispersion they induce. The unit also faces additional challenges and notably needs to increase the quality of its equipment and installations to remain competitive. These challenges are well addressed by the unit, which has made efforts to renew and/or acquire new equipment. Nevertheless, continued efforts must be made to improve working space. The research conducted by the IRFAC is very good to excellent with respect to the size of the unit. The director has an outstanding national recognition and some members are also well recognised at the national level.

The unit is proactive in the search for external funding which represents 80% of the available funds, not including institutional salaries. This is reflected in the excellent national grants obtained as leader by members (4 INCa, 1 ANR, 1 HU) although international funding is limited to training grants (e.g. 1 COST grant as partner). Even if the success rates for ERCs and international grants are low, the unit has the potential to participate in consortia, even if it does not carry the project.

Research carried out by the unit has some industrial applications (2 patents deposited) and three industrial contracts.

The unit is very good for training and three HDR were obtained during the current mandate. It has hosted 38 PhD (24 theses defended for 28 HDR), 54 trainees, six post-doctoral fellows. PhD students have authored 32 original publications.

The contribution of the unit to the dissemination of knowledge is good to very good: some members of the unit participate to charitable bodies, foundations and other learned societies; development of some courses for students; organisation of events for the general public. The involvement of a larger number of team members, and in particular PhD students, could strengthen these interactions with the general public and contribute to the development of some soft skills.

Overall, the national recognition of the unit is excellent regarding its involvement in research management (participation in national scientific committees) and the development of original research topics published continuously over the period in high quality journals.

DETAILED EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

During this contract, the unit increased the quality of its publications, publishing in very good (Frontiers Immunol. Oncogene, Cancer Letters...) to excellent or outstanding (J Exp Med, Cell Death Differentiation, Cancer Res, Clin Cancer Res, Elife, Blood, NEJM, J Clin Oncol) journals (44 articles as PI, 58 in collaboration).

Despite the geographical isolation of the site and the lack of investment in infrastructure, the unit has endeavoured to increase its attractiveness and to strengthen its staff with the arrival of statutory researchers (Inserm, 'Ligue National Contre le Cancer', university hospital) and contractual researchers (post-doctoral fellows).

The unit has been proactive in seeking financial support from the host institutions in order to implement structural changes compatible with current regulations and the pursuit of high-level research. They have acquired equipment including a cytometer analyser (LSR Fortessa X-20, BD Biosciences), a cell sorter (FACS MelodyTM, BD Biosciences) and a fluorescence microscope with an Apotome function for the acquisition of 3D images (APOTOME2, Carl Zeiss SA).

The unit is aware of the risk of dispersion due to the different research themes and model systems used, but the committee agrees that points of common interest are present and effort have been made by the unit during this contract. Nonetheless, there is still room for improvements on this aspect.

B – EVALUATION AREAS

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

Assessment on the unit's resources

The assessment on the unit's resources is excellent considering the increase in permanent staff and the integration of clinicians. Fund-raising has been excellent and the policy of pooling funds makes it possible to distribute funding among the teams. The unit has consolidated its activities into a single location and this is very satisfactory. However, some limitations still persist: the structural investments made on this site are insufficient in spite of a proactive policy of the unit to seek funds; infrastructures are still not up to the level of the scientific ambitions of the unit and negatively impact on its attractiveness.

Assessment on the scientific objectives of the unit

The scientific objectives of the unit are excellent and ambitious. They aim to understand how mechanisms hijacked from embryonic development and/or stem cell characteristics may explain the plasticity of cancer cells (and therapeutic responses). This plurality of questions is also reflected in the multitude of models and innovative technologies used.

Assessment on the functioning of the unit

As the committee did not perform interviews, its opinion on this subject only covers the actions taken in terms of health and safety, sustainable development and data security provided in the written document.

The unit has implemented all available means/tools (single document of professional risks, individual risk exposure sheet, health and safety register, newcomers' formations...).

Computer security is very good and ensured by the minimum necessary preventive measures and the use of software dedicated to back up. The unit is involved in a policy of sustainable development in various ways, whether in terms of waste management or encouraging staff to use soft means of mobility.

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

The unit currently has 65 members, including 23 clinicians. The unit hosted two fixed term contract staff and 43 permanent positions (2 CNRS, 7 Inserm, 1 Centre de lutte contre le cancer), 23 clinicians, 10 engineer technicians), fifteen PhD and three post-doctorate fellows. The staff increased during the current mandate: it was joined in 2020 by a third team which reinforces human and scientific potential; ten tenured research support staff arrived and 38 PhD students were trained (for a total of 28 HDRs) during the period.

Fundraising was obtained by the unit with ten national contracts (5 INCa as PI, 2 as partner; 2 ANR as partner, 1 PHRC as partner); Eleven host institution or regional funds (IDEX, Région Alsace, Cancéropôle), 33 grants from charities, as PI (19 LNCC, 5 ARC, 1 Ass Lorette Fugain, 1 Gefluc). These contracts represent a total of approximately 6 million euros and 80% of the unit's resources. The pooling of funds allows the three teams to operate in an equivalent manner.

Weaknesses and risks linked to the context

There are no European contracts for operating costs, the international grants (ECOS Nord x2, MITAC x2, Euridoc and Shanghai University grant) only covered travel costs and two fixed-term contracts (for 60 months).

Industrial, European and large project funding (Idex...) only represent 10% of the funds raised.

Investments made for the renovation of aging buildings (2.4M€ CPER grant) are not sufficient for optimal working conditions.

Numerous retirements are expected in the next few years and risk reducing the human resource potential. However, the lack of rehabilitation of the Inserm building considerably compromised the attractiveness of the laboratory and has resulted in the failure of projects aiming to increase interactions with other researchers.

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

Strengths and possibilities linked to the context

The unit's research is focused on three main axes: the study of a transcription factor (CDX2) in the initiation and progression of cancers through the development of original preclinical models (team 1); the role of the tumour microenvironment in the resistance to therapies in head/neck and gastric cancers (team 2), and the elucidation of mechanisms involved in colon cancer and in particular the role of two factors (TRa1 and the chemokine CXCL12) (team 3). Research conducted by the unit is mainly fundamental; however, with the arrival of clinicians the translational aspects will increase. The expertise of the three teams in each of their respective fields and models is excellent. The director of the unit and the team leaders are involved in numerous scientific bodies, which greatly contributes to the unit's visibility. The unit has access to the biological resources necessary for its research and is thus able to ensure continuity between basic and clinical research.

Weaknesses and risks linked to the context

The diversity of clinical models and scientific approaches poses a strong risk of dispersion, even within individual teams. The pathologies studied appear very diverse and extrapolation from one model to another is challenging. The links between clinical and basic research are not fully established, judging by the unit's publications. The contribution of clinical questions to the basic research of the unit is not yet apparent in the publications of the laboratory and vice versa.

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 deploys all the tools made available by the administrations (Inserm and University). Three persons (prevention assistants) are dedicated to the management of health and safety. The unit is aware of the impacts of its activity on its personnel and on the environment and has taken all necessary measures to limit negative effects. To do this, they use all the means made available by the host institutions (individual risk exposure sheet, health and safety register, AGIR software...).

The unit has put in place the necessary actions in favour of the environment (Controlled waste disposal in accordance with the university's services, waste sorting...) and sustainable development (encourage soft mobility (bicycle) and the train).

Weaknesses and risks linked to the context

Gender parity is unbalanced (M 21/F 13) for researchers and (M 4/F 9) for research support staff.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The overall attractiveness of the unit is excellent. This is reflected by the arrival of a promising new team from Lyon. The success rate in national competitive calls is excellent. However, while the attractiveness for PhD students is excellent, the recruitment of young scientists is moderate and no EU actions developed.

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

Members are regularly invited to present their work in national (not developed in the report) and international (not developed in the report) meetings on basic or translational science (5–10 meetings each team yearly). The members of the unit are involved in several scientific councils (ARC foundation, Société Française de Gastroentérologie...) or commission (Cell Biology commission of ARC foundation) and/or learned societies or charities at the national level and one is a co-leader of a COST Action. Unit members participated in the organisation of two international congresses (European Conference on Infections in Leukaemia, 1st Proteocure international meeting) and one of the members of the unit made two trips abroad as an invited professor – Mexico and China (2x 1 month). Unit members participate in four editorial boards of scientific journals (Medical Mycology Journal, Current Fungal Infection reports, Cancers. Advances in Head and Neck Squamous Cell Carcinoma Special edition). Members of the unit preside and/or take part in research steering or scientific expertise bodies at the international (Swiss Cancer League, Worldwide Cancer Research, Israel Ministry of Science, Israel Science Foundation, Austrian Science Funds, American Society for Pharmacology and Experimental Therapeutics) and national level (ARC foundation, FHU program, LYSA, FILO, ANR...).

Weaknesses and risks linked to the context

The international visibility is not sufficiently demonstrated through the lack of EU grants and participation to networks.

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

Strengths and possibilities linked to the context

The recruitment of the unit is dynamic when considering recruitment of students (3 to 5 masters 2 and 2 to 5 thesis students per year). PhD students are all funded by 'ministère de l'enseignement supérieur et de la recherche' and other supports (Région Grand-Est, FRM and Ligue contre le Cancer (2x)). Teams 1 and 2 have been reinforced by the arrival of three researchers and seventeen clinicians. The unit was also strengthened by the arrival of a third team.

Communication between team members is ensured by regular meetings between researchers and students: a weekly meeting to present experimental results and bi-monthly meeting devoted to the progress of research projects. Students also have to refer to their supervisor on a daily basis to discuss results and to ensure that experiments and their analysis are carried out according to established rules. Everything is recorded in laboratory notebooks or labguru.

Weaknesses and risks linked to the context

The unit did not host any guest researcher during the period. There are only three post-doctoral fellows from abroad (2 from China, 1 from Lebanon)

The contribution of PhD students to research projects is not sufficiently reflected in the production of first author publication in high-profile journals. Among the theses defended over the period (24), only eight PhD students have published original articles as first author and two have not been published at all.

Research publications during the period do not attest to the involvement of clinicians in the main research projects of the Unit.

Retirement of senior members may cause a loss of human and scientific potential.

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

Strengths and possibilities linked to the context

The unit is involved in future investment programs (1 ITI, 2 IDEX) and was the leader of excellent national calls (4 Inca grants) and partner of two Inca, 2 ANR, two ITMO and 1PHRC grants. It also received, as PI, 39 grants from local authorities and charities (ARC foundations, FRM, Ligue contre le cancer). The unit also obtained, as co-coordinator, international competitive training grants (e.g. COST).

The attractiveness of the unit is also reflected in the number of student trainees: Thirty-eight PhD students were trained during the period, 24 defended. Eighteen students were able to secure competitive funding through the doctoral school and twenty through other funds (ANR, Région Grand-Est, FRM and Ligue contre le Cancer).

Weaknesses and risks linked to the context

No major weaknesses have been identified.

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

Strengths and possibilities linked to the context

For its activity, the unit relies on scientific platforms in Strasbourg and its region as well as elsewhere in France and Germany. Nevertheless, the unit has developed two in-house facilities dedicated to PDX and preclinical studies. Five people are trained to use the common equipment and platforms. During the 2016–2021 period one cytometer, one cell sorter, one fluorescence microscope and one microscope were funded through calls of tenders.

Weaknesses and risks linked to the context

Human resources dedicated to technical platforms are not secured with a team comprising only one engineer and two zootechnicians.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The quantity and quality of the unit's original publications (44 as PI in Elife, Cancer Res, J Exp Med, ... and collaborators in Nature, Annals Oncol). are excellent considering the size of the unit. Published work is in adequacy with the international standards of the scientific disciplines and the laboratory is in line with a proactive approach on scientific integrity and ethics. All the work is not yet published in open access journals.

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

The unit's publications are in compliance with international rules of probity and ethics. The unit have published in general scientific publication as PI, in good to very good journals (Oncogene, 2 Cancer Letters...) to excellent (1 Elife, 1 J Exp Med, 1 Cell Death and Differentiation, 1 Cancer Res, 1 Leukaemia, 1 Development...) or outstanding quality (1 Ann Oncol, 1 Nature in collaboration) journals. There is a strong publication activity in

clinical research journals (396 papers, 127 as PI). Twelve publications are in common between team 1 and team 2.

Weaknesses and risks linked to the context

No major weaknesses have been identified

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

Considering the stage of the career, the scientific production is shared between seniors team members. For clinical publications, the number of published articles is 396, 127 as PI.

Weaknesses and risks linked to the context

PhD students are not sufficiently represented in publications. Only 8 out of 24 theses defended are associated with the publication of an original article as first author. The ratio of defended PhD (24) to the number of HDR (28) is low.

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 unit fully respects the rules and values set forth by national and international organisations to ensure the probity and ethics inherent in scientific work. Human primary samples are obtained according to the procedure approved by the institutional review board of the Strasbourg University Hospital and the CPP ('Comité de Protection des Personnes'). The access to samples of human embryos after voluntary termination of pregnancy has been approved by the Institutional Review Board of Inserm (IRB00003888, IORG0003254, FWA00005831) under the number 21-854.

Weaknesses and risks linked to the context

The strategy for long-term secure storage of research data and implementation of backup storage is not well described in the written document. Portable hard drives are not the best strategy for this type of storage.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The overall interactions between the unit and non-academic partners are very good to excellent. On the technology readiness level (TRL), the work of the unit would be at levels 3-4 which is in accordance with research activity of the unit.

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

Strengths and possibilities linked to the context

Interaction with industry applied for this unit: three industrial contracts were obtained with StemCell, Anagenesis and Biocodex. This research would be at level 3 or 4 on the TRL scale allowing two patent deposits. The presence of clinicians in the unit favours the obtention of industrial contracts.

Weaknesses and risks linked to the context

There are no spin-offs or start-ups from the unit.

The contribution of the unit to the non-academic world is very heterogenous among teams and overall remains limited in industrial contracts and the implication of clinicians.

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

Strengths and possibilities linked to the context

NA

Weaknesses and risks linked to the context

NA

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

Strengths and possibilities linked to the context

NA

Weaknesses and risks linked to the context

NA

C – RECOMMENDATIONS TO THE UNIT

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

The unit may continue to apply for competitive grants. Integration of clinicians in the unit is an asset and the unit may work on improving their integration in research activities. The unit should focus on main research models in coherence with the available human resources.

Recommendations regarding the Evaluation Area 2: Attractiveness

The unit may develop strategies to attract and/or allow the emergence of young scientists in the unit. The unit may increase visibility by inviting international scientists.

Recommendations regarding Evaluation Area 3: Scientific Production

The unit has to continue in its effort to publish in high-profile papers.

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

The unit should implicate the whole staff to increase their communication actions.

TEAM-BY-TEAM ASSESSMENT

Team 1: Intestinal identity: from stem cells to pathology
 Name of the supervisor: Mr Jean Noel Freund

THEMES OF THE TEAM

The aim of Team 1 is to investigate cancer initiation and progression. Research is focused on the gut-specific transcription factors CDX2 in intestinal cancers as well as in situations of abnormal ectopic expression in malignancies of the upper digestive tract (pancreas, stomach), and also in leukaemia. Both systems share common properties (i.e. dynamic homeostasis based on active stem cells, common genes involved in embryonic development and tumorigenesis). Team 1 has access to human primary samples from malignant and inflammatory diseases and human embryonic samples. It has developed conditional Cdx2 knockouts and ectopic/overexpression mouse models that allow the generation of several innovative models of tissue-specific, inducible expression of Cdx2 in various tissues. The team uses state-of-the-art techniques – i.e. high-resolution imaging, lineage tracing (sc) RNAseq ... –.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

To address previous recommendations and in particular to develop a new axis in onco-haematology, Team 1 acquired new equipment to set up a cytology platform equipped with a cytometer analyser, a cell sorter and a fluorescence microscope with an Apotome function for the acquisition of 3D images. Although the previous committee was concerned by the lack of focus on the haematopoiesis project, the team has demonstrated its capacity to succeed by their publications (1 Leukaemia, 1 Blood during the last mandate).

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	1
Scientist (Chargé de recherche, CR) and associate	4
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	3
Subtotal permanent personnel in active employment	18
Non-permanent teacher-researchers, researchers and associates	4
Non-permanent research supporting personnel (PAR)	3
Post-docs	1
PhD Students	6
Subtotal non-permanent personnel	14
Total	32

EVALUATION

Overall assessment of the team

Team 1 focused on intestinal cancers, approached from the perspective of embryonic developmental mechanisms that are hijacked during the tumour process. The published work is excellent (J Exp Med, Blood, Leukaemia, Cell Death and Differentiation...). The team leader has an outstanding national visibility and the team's fundraising ability is excellent (3 INCa, 1 ANR). Although two researchers and seven clinicians-teachers-researchers joined the team in 2018, the team is facing many retirements (5 researchers will reach the legal retirement age during this contract). Replacing team members is an issue of concern to the team. The overall attractiveness of the team is excellent.

Strengths and possibilities linked to the context

During this period the team hosted one post-doctoral researcher and trained eighteen PhD students (13 theses defended and 5 theses in progress)

Members of Team 1 are invited to present their work in national and international meetings on basic and translational research (5–10 each team yearly).

The team leader's actions in the scientific community are remarkable: Member of the Organizing Committee of the JFHOD international meeting (Paris) more than 5,000 scientists and MDs); organiser of the 1st Summer School of the Innovac institute (2021) and the Journée Scientifique Annuelle de la Conférence de Coordination Interrégionale du Grand Est de la Ligue contre le Cancer (CCIRGE-LCC). He is also a member of several Scientific Boards: Fondation ARC CN3, as Vice-President (2019–2020) and President (2021–2022); (SNFGE) (2012–2021); FHU-ARRIMAGE (2018-2023) ; ITI-Innovac (2020–2024). One member of the team (PUPH) was on the Organizing Committee of the ECIL (European Conference on Infections in Leukaemia) in 2019 and in 2021, and of the Scientific Committee of the 9th Trends in Medical Mycology (Nice-Acropolis, 2019). Two CRs are members of the Scientific Board of the CECED. One PUPH is a member of the Scientific Boards of the Lymphoma Study Association (LYSA) and of the French Innovative Leukemia Organization (FILO).

The team had an excellent success rate in highly competitive national grants (promoter of 2 INCa grants and partner of three INCa and 1 ANR grant) and one international funds (Euridoc, (Trinational PhD Program in Immunology). It also received financial support, as project leader from Cancéropôle Grand-Est, ARC Foundation, Société Nationale Française de Gastroentérologie, among others. It was also a partner of the EURIdoc program, and involved in FHU ARRIMAGE and ITI Innovac.

The scientific production of this team is also excellent: 49 original scientific publications (19 as PI) among which eight in journals of excellent (J Exp Med, Cell Death and Differentiation, Clin Cancer Res, Blood, Leukaemia, Biomaterials...) and more than 200 clinical articles, some of which in outstanding journals (J Clin Oncol, Lancet Hematol, Gastroenterology). The team has developed excellent international collaborations, e.g. Barts London, UK, Hubrecht Institute (resulting in 9 articles), India (non-coding RNAs); Italy (haematopoietic development) and Germany (biomaterials).

One researcher has an industrial contract with Biocodex (2020–2022, 188 k€, 1 post-doctorate funding). Team 1 is involved in the dissemination of results – e.g. yearly during the Ligue contre le Cancer Bas/Haut-Rhin day, or the ARC Young Scientists Day, open to scientists and to donors, and for which the unit's director was co-organiser.

Weaknesses and risks linked to the context

The ratio PhD defence to HDR is low: 13/13, which correspond to one PhD per member in five years.

Team 1 is composed of eight permanent DR/CR/Eng-Tech and with eleven Clinicians, but its size will rapidly decrease due to the retirement of five researchers.

Only one post-doctoral researcher is currently hosted in the team which limits the access to new expertise.

The involvement in European/International grants is limited. No foreign trainee was hosted.

RECOMMENDATIONS TO THE TEAM

The committee acknowledge the excellence in the research activity and encourage the team to continue to publish in excellent journals and to participate in international consortia.

The committee also encourage the team to try attracting promising young scientists who could succeed with Inserm/CNRS Researcher applications.

Team 2: Mechanisms of the molecular stress response in the digestive system and pathologies

Name of the supervisor: Mr Christian Gaiddon

THEMES OF THE TEAM

The aim of Team 2 is to identify the molecular mechanisms underlying therapeutic response/resistance of aerodigestive tumours, with a specific focus on p53-like pathways. They also aim to use this information to identify novel therapeutic point of intervention and biomarkers for patient stratification, with a specific interest in gastric cancers that demonstrate a poor prognosis and limited therapeutic options.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Team 2 has addressed most of Hcéres recommendations. Specifically, they have refocused part of their research on gastric cancers, which may lead to innovative research and higher quality scientific production. Although there is still a lack of high-profile papers, they have developed comprehensive studies describing innovative mechanisms of cancer progression and treatment response that should overcome this weakness. In addition, they continue their efforts to publish in very good to excellent Chemical/Biology journals in their domain of expertise. Nonetheless, their research projects remain dispersed in three different tumour types, which may affect the progression of their research program.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	8
Lecturer and associate lecturer	2
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	3
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	4
Subtotal permanent personnel in active employment	18
Non-permanent teacher-researchers, researchers and associates	8
Non-permanent research supporting personnel (PAR)	0
Post-docs	1
PhD Students	7
Subtotal non-permanent personnel	16
Total	34

EVALUATION

Overall assessment of the team

The main scientific production is very good (interesting questions in cancer biology and therapeutics, with a specific interest in gastric cancers with therapeutic need.); the capacity to obtain funding is excellent (INCa, ITMO cancer as leader), thanks to the integration of research clinicians. The overall link with the private sector is excellent, as demonstrated by two patents and two contracts with industry (StemCell, Anagenesis) and solid interactions with chemistry labs. Nonetheless, a strong dispersion in the lines of research pursued persists (too disperse for the size of the team). In light of these elements, the overall attractiveness of the team is very good.

Strengths and possibilities linked to the context

The team has gained complementary expertise in cancer by the integration of clinical scientists with a specific expertise in aerodigestive cancers. The team obtained several national grants: two ITMO cancer grants, one ARC foundation program and one PHRC grant, as leader. The team also demonstrates the capacity to attract PhD students locally, with eight being supported by doctoral school fellowships and two from the la Ligue contre le cancer charity over the six-year period. Six PhD theses have been defended and seven are in progress.

In addition, their current collaborative network with chemistry laboratories at the national and international level enabled international grant rewards (ECOS, Proteocure, COST, MITACS), and visibility of the team in the domain, as shown by the invitation of the PI to international meetings (e.g. p53 family, metal-based anticancer drugs meetings) and invitation to write reviews in very good journals in the domain (Chem Soc Rev, Chem Rev).

The team contributed to 53 publications in good to very good basic/translational journals and 200 clinical articles, thanks to the integration of clinicians in the team. Most of these were as co-author. Fundamental research articles of the team were published in good to very good biological journals, including a paper signed by the team leader in a senior position (Elife, Cancer letters, Molecules, Cancers...). The team also published one research paper in an excellent chemistry journal (Chem Sci) over the period. Finally, several clinicians of the team contributed to translational/clinical works published in top journals (Nature, Lancet, NEJM).

The overall link with the private sector is excellent, as demonstrated by two patent licenses and two contracts with the industry (StemCell and Anagenesis) over the last years, thanks to a long-term interaction with chemistry labs.

Weaknesses and risks linked to the context

The research activity lacks sufficient focus and is dispersed over three distinct cancer types. Addressing their main biological question in such different biological systems requires a high level of resources for the current size of the team.

The team did not publish their research in high-profile journals of the domain yet. Nevertheless, the team has developed comprehensive studies describing innovative mechanisms of cancer progression and treatment response to be submitted soon, which should address this weakness.

The attractiveness of the team is not demonstrated by sufficient recruitment of post-doctorate fellows or fundamental young scientists during the contract (1 postdoc over the 5 years period).

The competition of some aspects of the research activity is high (p53 pathway) or increasing (biology of gastric cancer), which could impact on the success of some research projects.

RECOMMENDATIONS TO THE TEAM

The committee encourages the team to continue securing competitive grant applications. It supports and encourages the team's efforts to publish in high-profile journals and to interact with the industry. However, the committee suggests that the team should attract more young researchers (postdocs) and focus on one or two tumour types to ensure its international competitiveness.

Team 3: Development, cancer and stem cells
 Name of the supervisor: Mme Michela Plareroti

THEMES OF THE TEAM

Team 3 works on colorectal cancer. Their aim is to better understand the regulatory networks governing gut stem cells homeostasis and their contribution to neoplastic transformation. Their project also takes into account functional interactions between intrinsic factors of intestinal pathophysiology and external signals. The team showed the involvement of thyroid hormones, acting through the TRa 1 nuclear receptor, in the regulation of intestinal epithelium precursor cell homeostasis in both physiological and pathological (colorectal tumorigenesis) conditions. They also showed that the CXCL12 chemokine and its receptors CXCR4 and CXCR7 are involved in metastatic colorectal dissemination.

The team leader joined the UMR-S1113 in September 2020. One Member of team 1 integrated team 3, based on closely related research questions on colorectal cancer. Accordingly, two excellent publications are co-authored by members of Team 1 and 3 (Cancer Res, Development).

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Team 3 is a new team that was created in September 2020 and was therefore not evaluated per se during the previous Hcéres report.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
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)	0
Research supporting personnel (PAR)	0
Subtotal permanent personnel in active employment	1
Non-permanent teacher-researchers, researchers and associates	3
Non-permanent research supporting personnel (PAR)	1
Post-docs	1
PhD Students	3
Subtotal non-permanent personnel	8
Total	9

EVALUATION

Overall assessment of the team

Since the team joined the unit recently, the scientific production and the successful of this integration in IRFAC cannot be evaluated by the committee.

Strengths and possibilities linked to the context

NA

Weaknesses and risks linked to the context

NA

RECOMMENDATIONS TO THE TEAM

NA

CONDUCT OF THE INTERVIEWS

Date(s)

Start: NA

End: NA

Interview conducted: None

INTERVIEW SCHEDULE

There was no interview

PARTICULAR POINT TO BE MENTIONNED

The committee worked uniquely on the scientific document because the meeting was cancelled by Inserm

IMPORTANT MESSAGE :

Lors de la phase de préparation de cette évaluation, la tutelle Inserm de l'UMR a informé le Hcéres et ses experts que l'unité, confrontée à une situation déstabilisante traitée par l'autorité judiciaire, ne se trouvait plus dans des conditions propices à la tenue de son évaluation dans les conditions habituellement pratiquées par le Hcéres. D'un commun accord, il a été convenu qu'à titre exceptionnel l'évaluation de l'unité serait conduite sur la seule base des documents écrits fournis aux experts.

This report was made based on the scientific documents provided only.

GENERAL OBSERVATIONS OF THE SUPERVISORS

Université

de Strasbourg

Monsieur Éric Saint-Aman
Directeur du Département d'évaluation de la recherche
HCERES - Haut conseil de l'évaluation de la recherche et
de l'enseignement supérieur
2 rue Albert Einstein
75013 PARIS

Strasbourg, le 9 juin 2023

Objet : Rapport d'évaluation DER-PUR230023185 - IRFAC - Interface recherche fondamentale et appliquée en cancérologie

Réf. : RB/FF/ 2023-438

Rémi Barillon

Vice-Président Recherche,
Formation doctorale et Science
ouverte

Cher Collègue,

Affaire suivie par :

Florian Fritsch
Responsable du département
Administration de la recherche et
accompagnement des chercheurs
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L'université de Strasbourg vous remercie ainsi que tous les membres du comité HCERES pour le travail d'expertise réalisé sur l'unité de recherche « Interface recherche fondamentale et appliquée en cancérologie » (IRFAC – UMR_S 1113).

Nous n'avons aucune observation de portée générale à formuler sur le rapport d'évaluation transmis.

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

Rémi Barillon



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valorisation**

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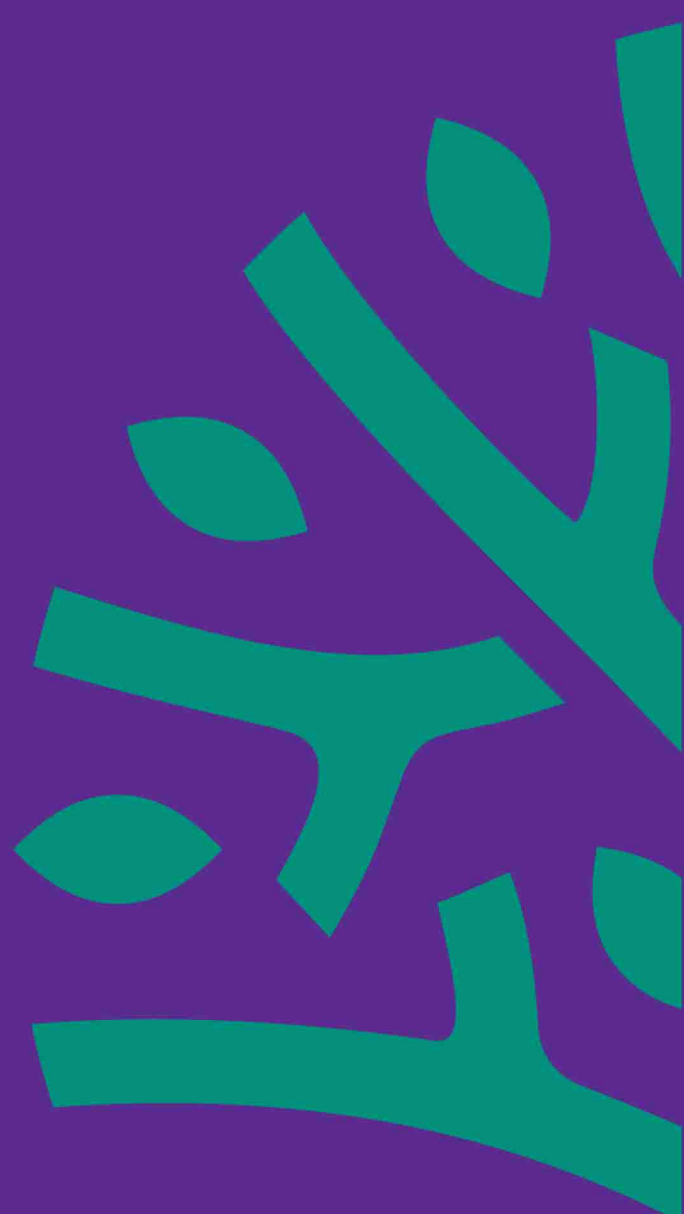
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