Research evaluation

EVALUATION REPORT OF THE UNIT

CRCM – Centre de recherche en cancérologie de Marseille

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

INSERM DR 2 PACAC
CNRS DR12
Aix Marseille Université
Institut Paoli Calmettes
CLCC

EVALUATION CAMPAIGN 2022–2023
GROUP C

Report published on May, 10 2023

In the name of the expert committee[1]:

Yolanda Prezado, Chairwoman of the committee

For the Hcéres [2]:

Thierry Coulhon, President

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

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

MEMBERS OF THE EXPERT COMMITTEE

Chairperson:	Mrs. Yolanda Prezado, CNRS, Orsay Vice-chairperson: Mr. Philippe Valet, Université Toulouse 3 — Paul Sabatier — UPS, Toulouse
Experts :	Mrs. Virginie Lafont, Inserm, Montpellier Mr. Frederic Boccard, CNRS, Gif-sur-Yvette Mrs. Véronique Maguer-Satta, CNRS, Lyon (CNRS 24) Mrs. Nadira Delhem, Université de Lille (CNU 65) Mr. Claude Sardet, CNRS, Montpellier (CSS 2) Mr. Niclas Setterblad, Sorbonne Paris Cité, Paris (supporting personnel) Mrs. Françoise Ochsenbein, CEA, Gif-sur-Yvette, Mrs. Virginie Penard-Lacronique, Inserm, Villejuif, Mrs. Anabelle Decottignies, Duve Institute/UCLouvain, Brussels Mr. Sebastien Papot, Université de Poitiers

HCÉRES REPRESENTATIVE

Mrs. Sophie Ezine

CHARACTERISATION OF THE UNIT

- Name: Centre de recherche en cancérologie de Marseille
- Acronym: CRCM
- Label and number: UMR 1068, UMR 7258, UMR 105
- Number of teams: 20
- Composition of the executive team: Mr. Jean-Paul BORG

SCIENTIFIC PANELS OF THE UNIT

SVE: Life, Health and Environmental Sciences

SVE6: Human Physiology and Physiopathology, Aging

SVE3: Living Molecules, Integrative Biology (From Genes and Genomes to Systems), Cell and Development Biology for Animal Science
SVE4: Immunity, Infection and Immunotherapy
ST4: Chemistry

THEMES OF THE UNIT

The *Centre de Recherche en Cancérologie de Marseille* (CRCM) is organized in 22 research teams supported by eighteen research platforms, the CRCM addresses (i) basic aspects of cancer initiation and development by identifying molecular alterations and understanding their functional consequences; (ii) tumoral microenvironment and immune system and (iii) translational and clinical research to identify prognostic and diagnostic biomarkers and to launch innovative clinical trials.
The CRCM targets the cancer field through comprehensive and innovative research programs based on the expertise of researchers, clinicians and engineers. The research activities are divided into seven major scientific axes including Genomic Instability; Signalling, Cell Polarity and Cell Migration; Tumour Heterogeneity; Cancer Stem Cells; Immunotherapy; Therapeutic Antibodies and Small Molecules; Precision Medicine, with strong inter-team interconnections.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The CRCM, created in 1972 (as a first Inserm laboratory 'Carcinogenesis polyoma virus and melanoma' at Institut Paoli-Calmettes) with twenty researchers in the '70s to 250 in 2012 and 400 in 2018 is located over three geographically separated locations: the main one is Institut Paoli-Calmettes, (IPC), 15% of the CRCM people in Luminy (Science Faculty campus) and 2% in la Timone (Pharmacy Faculty campus). Taken together, these locations are interconnected by twenty minutes driving.

RESEARCH ENVIRONMENT OF THE UNIT

The CRCM exhibits strong and synergistic commitment of the supporting institutions at the financial, administrative, infrastructure, scientific and technological levels. The centre is supported by four managing bodies: Aix-Marseille-Universities (AMU), INSERM, CNRS and IPC. The Région PACA, Ville de Marseille, Métropole and IPC supported 2 Contrats Projet Etat-Région (CPER, 2015–2020, 2021–2025) dedicated to renovate a 3,000 m2 building on the IPC site and to host the pancreatic cancer program, platforms and new teams (CPER 'Fight Cancer': budget: 11 M€, delivery date: 2024).
The CRCM was involved in two European International Training Networks in the areas of cancer signalling; has established a collaboration with the Cancer Research UK Oxford Centre since 2018; a collaboration was also established with the Genome Sciences and Precision Medicine Center of the University of Michigan. It also benefited from two *Investissement d'Avenir*: The Pioneer project (https://marseille-immunopole.org/the-pioneer-project/) and The MImAbs consortium (http://www.mimabs.org/fr/).
The CRCM and IPC, research teams are working with other immunology and research centres within the Cancer & Immunology Institute (created by AMU in 2019). IPC and the CRCM are also members of the Universitary Marseille Imaging Institute and the Universitary Institute for Artificial Intelligence. They are also part of the CALYM and OPALE Carnot Institutes focused on the organisation of research and innovation on lymphoma and leukaemia, respectively. Five of the eighteen Coretech platforms have been awarded a label by the French Infrastructure Biology and Health (IBiSA) agency.
Since local/national institutions are supportive and CRCM is involved in numerous national/international networks, the global environment of the unit is in favour of increasing scientific development and the value of both teams and platforms.

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

Permanent personnel in active employment	
Professors and associate professors	47
Lecturer and associate lecturer	23
Senior scientist (Directeur de recherche, DR) and associate	26
Scientist (Chargé de recherche, CR) and associate	34
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	108
Subtotal permanent personnel in active employment	**238**
Non-permanent teacher researchers, researchers and associates	39
Non-permanent research supporting personnel (PAR)	34
Post-docs	46
PhD Students	93
Subtotal non-permanent personnel	**212**
Total	**450**

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

Employer	**EC**	**C**	**PAR**
Inserm	0	49	55
Institut Paoli-Calmettes	17,5	8	38
Aix-Marseille Université	34	4	21
CNRS	0	28	14
CHU Marseille	16.5	0	1
INRIA	0	2	0
Others	0	12	6
Total	**68**	**171**	**135**

UNIT BUDGET

Recurrent budget excluding wage bill allocated by parent institutions (total over 6 years)	**7,721**
Own resources obtained from regional calls for projects (total over 6 years of sums obtained from AAP idex, i-site, CPER, territorial authorities, etc.)	6,196
Own resources obtained from national calls for projects (total over 6 years of sums obtained on AAP ONR, PIA, ANR, FRM, INCa, etc.)	44,128
Own resources obtained from international call for projects (total over 6 years of sums obtained)	3,414
Own resources issued from the valorisation, transfer and industrial collaboration (total over 6 years of sums obtained through contracts, patents, service activities, services, etc.).	4305
Total in K euros	**65764**

GLOBAL ASSESSMENT

The CRCM, composed of seventeen teams, is the leading research cancer in the PACA region. It is a multidisciplinary cancer research centre co-runs by the INSERM, the CNRS, the University of Marseille and the Cancer Hospital Paoli-Calmette (UNICANCER federation) where scientists and clinicians are working side-by-side to advance knowledge into fundamental biological processes in cancer and are developing innovative therapeutic approaches for patient benefit.

The unit produced excellent research publications (2,647 scientific papers of which a percentage of 75% were published in the better journals in their field of expertise and most of them in the most notorious disciplinary journals). Some research articles are even published in prestigious multidisciplinary journals (e.g.: Nature 2016 and 2019).

The attractiveness of the unit is excellent. The unit's members have been highly successful in obtaining funds, with a majority (> 80%of the unit's funds coming from external origin) of national origin (40 ANR grants, 85 INCA grants, etc.) and 41 contracts financed by territorial authorities (i.e. PACA) or by University or national Excellence programs (Région PACA, IDEX AMU and PIA), 13 *Investissements d'Avenir* contracts (PIA), 150 contracts funded by foundations and charities (ARC, FRM, LNCC, GEFLUC, FDF, Laurette Fugain, etc.). Several teams obtained the competitive 'Équipe FRM' or 'Équipe LNCC' labels. Although the success in European calls has been lesser, the CRCM is involved as a partner in twelve international contracts, including seven European ones (4 as coordinator).

While globally the CRCM members received a good number of invitations to contribute to international congresses, the attractiveness of some teams still needs to be improved by increasing the number of invitations to international conferences as speakers and as members of the scientific committee or organising committees.

The CRCM has demonstrated an excellent capacity to attract new high-level teams. In the last calls, three new teams were created. This indicates an excellent international recognition, but that could be significantly improved by coordination of European grants or consortia. The involvement in research training and teaching are very good with 92 members of CRCM having an HDR. About 163 PhDs were defended and 81 postdoctoral fellows have been hosted in CRCM teams. The recruitment of the best PhD students could be improved at the local, national and international levels by increasing the visibility of the centre for master students.

The unit has made major efforts to mutualise technological resources by creating eighteen platforms with very innovative technologies, staffed by high-level permanent and non-permanent engineers and technicians. The IBISA label regards only five over eighteen and could be improved. The ISO9001 certification could also to be obtained for more platforms. In general, the unit must be attentive to the sustainability of the economic model, and of the prioritisation of their few state-of-the-art platforms and of their numerous other technical facilities. With regard to interactions with the non-academic world, CRCM teams translated their research by filling more than 100 invention declarations, it has been involved in start-up creations (5), the set-up of clinical trials (24) and signed24 R&D projects with the industrial companies.

The organisation of the unit and laboratory life revealed weaknesses in gender parity (3 women team leader/17 teams) and communication strategies.

The committee assessed seven teams as outstanding, one as excellent to outstanding, eight as excellent and one very good to excellent. The continual striving to enhance CRCM visibility, publish in the best journals, apply to international grants, and recruit high-profile new teams, within the next quinquennium, should continue to ensure its path on an upward trajectory to reinforce its position as a leading Cancer Centre in France, with also a strong potential, still too little exploited, to position itself at the European level.

Overall, we rate CRCM as 'excellent to outstanding'.

DETAILED EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Previous HCERES report contained three main recommendations:

1. *The CRCM should recruit high-level postdocs*. The scientific appeal of the unit should be paralleled with good procedures to help candidates from outside Marseille to settle in the region. This would entail a regular update of the website, job postings… Moreover, *increase attractiveness*: the unit needs to increase the recruitment of high-level students and postdoctoral fellows and improve the level of proficiency with the English language. The CRCM has endeavoured to amplify both its insertion in the academic world and to make its training offer more visible. It is involved in the training and research institutes that AMU has recently set up, in particular the Cancer& Immunology Institute (ICI), and the Marseille Imaging and Laennec Institutes (Digital Sciences & Artificial Intelligence). The unit trained 22 master students per year and a total of 163 PhD students. However, the recruitment of PhD students in fundamental research aspects is still low and should be improved. The unit implemented a proactive strategy to attract internationally recognised researchers through open calls. Recently, in 2020 and 2021 two new teams were recruited via a selection made by the SAB. Despite the fact that the unit has set up regular seminars in English, most meetings are only in French and the administrative staff is not proficient in English language. The unit spent some efforts on improving their website.
2. *The partnership of CRCM with the IPC is crucial to the future success of this unit, but to bring this to the next level requires that both entities agree on a combined strategy to tighten the connections between the basic and clinical research programs*. The current level of interactions are excellent, considering the short time the unit has been up and running, but much of the basic research is not yet connected to clinical activities. Thus, a strategy that brings the basic and clinical research programs closer together would improve the chances that innovative therapies can be developed. The interaction with IPC has been enhanced by creating three translational programmes involving actors of both sides along with protected time for clinicians as well as the creation of a Translational Research Committee including IPC clinicians and CRCM researchers. The unit has taken care of optimising the data transfer between CRCM/IPC and on the valorisation and optimisation of the existing annotated biobanks.
3. *The unit will have to develop a strategy to prevent that crucial knowledge will disappear from the unit, because it can no longer sustain the contract of well-experienced researchers or engineers. This problem is not particular to this unit, but poses a threat to the competitiveness of the French research system as a whole*. To face the problem of the retention of expertise, the unit has made great efforts to develop open access platforms. The support is provided collectively to these platforms by the CRCM and the IPC, including of human resources, and their new organisation in a CoreTech. Importantly, the CRCM recruited nine junior researchers, one senior researcher and four ITA staff on permanent positions.

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 regarding scientific production and fund attraction, although more Europeans funds are desirable. The plans to set up a 'Europe unit' managed by a researcher in reconversion could help increase the access to European funds. The unit has excellent technological resources (Coretech), some of them understaffed which risks a future suboptimal functioning. Their economic model is reaching its limits. The unit is well established and anchored in the local environment.

Assessment on the scientific objectives of the unit

The assessment on the scientific objectives of the unit is excellent. The unit has defined specific objectives addressing an important health problem (cancer) and in line with the governing bodies. Special efforts were made to increase the translational vision and the international attractiveness. On top of producing research publications, it is involved in the creation of start-ups and set up of clinical trials.

Assessment on the functioning of the unit

The unit has a very good functioning, articulated in several committees. Communication and parity aspects are to be improved. The unit has started making efforts in that direction by creating Parity and Professional Equality, R6Lab (sustainable development) and PSR Committees have been created.
The unit should be congratulated on their efforts to establish a data management program and suitable storage solutions. The unit regularly updates a business continuity plans to cope with any emergency situations.

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

Strengths and possibilities linked to the context

The unit has an adequate profile to its missions and globally adequate human resources (422 staff members, 52% tenured positions, 80 of them researchers and teacher researchers and 12% of clinicians, organised in 17 teams).
The unit was able to recruit two new teams.
The unit is able to attract external financial resources, with a majority (> 80% of the unit's funds, salaries not included) of local (i.e. Cancerolopole PACA), national origin (40 grants fromANR, 85 from INCa…) as well as foundations and charities (such as ARC, FRM…). The plans to set up a 'Europe unit' managed by a researcher in reconversion could help increase the access to European funds.
To effectively achieve its goals, the unit has made a great effort mutualise the common efforts and keep the 'savoir-faire' by creating eighteen platforms at the disposal of the members of the unit under the supervision of a researcher and managed by one engineer, as well as, towards regrouping the platforms into a Coretech. The platforms were created in coherence with the scientific objectives of the unit. The unit employs one third of its recurring endowment to finance the Coretech's eighteen platforms.
The unit is anchored in the local environment, with tight relationships with the IPC hospital (important for clinical translation), and local institutes of immunology, imaging, as well as other important players in the regional Canceropole and AMU.
The potential integration of the unit in the European University and the IA Laennec Institute can help improve its international visibility and attractiveness (especially important to attract mathematicians).
The unit space has been increased to be in coherence with the activities. Yet, the unit was distributed in three sites, which does not facilitate exchanges. Certainly, the delivery of the Fight Cancer building (Q1 2023), allowing

the integration of the Luminy site teams on the IPC site (geographical rapprochement), and the redeployment of certain platforms will smooth internal exchanges.

Weaknesses and risks linked to the context

The geographical dispersion of the unit, divided in three sites, represents a risk for fluid interactions and internal communications as it is difficult to create interactions and foster interdisciplinary.
The efforts on creating a data management plan and storage solutions risk being ineffective if not accompanied by a clear institutional strategy on data storage and management.
The important efforts in creating platforms and Coretech are not accompanied by an adequate number of permanent personnel, risking a suboptimal functioning of the platforms and the loss of personnel with know-how.
The IBiSA label and the ISO9001 certification are associated with a few number of platforms.
The administration is understaffed (10 persons, 2% of the personnel), risking a smooth unit functioning, especially critical in the current 'growing' phase of the unit.

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 has well-defined scientific objectives and has worked towards their achievement. The objectives are globally relevant with respect to the state of the art.

The unit is globally well connected with relevant academic and non-academic players. The scientific objectives of the unit have a clear societal impact since they address a major health problem, cancer treatment. The presented objectives are in line with those of the supervisory bodies. As a result of its activities, the unit's production consists of research publications, patents (more than 100 invention declarations) and start-up creation (5).

Weaknesses and risks linked to the context

The main weakness and risks associated with the context are the following:

- The communication and direct link with the four supervisory boards (Aix-Marseille-Universities –AMU–, INSERM, CNRS and Institut Paoli-Calmettes – IPC) is not always administrative fluid and straightforward.
- The research themes of the unit requires access to cutting-edge technologies (such as next generation sequencing or automated immunochemistry), for which the institutional investment remains low in France

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 complies with the regulations and principles of human resources management. With that aim, a Parity and Professional Equality Committee has been created. Among others, the unit has encouraged women to take responsibility positions. Still the proportion is very weak. The unit has taken care of preventing psychosocial risks (PSR), and has created a committee on PSR. Every newcomer is adequately informed on the internal rules and regulations. To comply with the recommendations on environmental risk prevention and the pursuit of sustainable development goals an R6Lab (6 R rules: reduce, recycle, reuse, replace, repair, re-educate) committee was created in 2021 and validated by the centre's direction. Its main mission is to take stock of the situation and to set precise objectives to reduce their environmental footprint.

Weaknesses and Risks linked to the context

The unit lacks a clear institutional strategy on data storage and management, especially critical in this unit which generates enormous amount of data. The internal communication within the unit is still to be improved.
Parity aspects have to be considered.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The unit has an excellent attractiveness as reflected by the excellent funding obtained, numerous collaborations, and the successful recruitment of new high-level teams. The high-level technological support, staffed by high-level engineers and technicians, in spaces of excellent quality, is a very attractive asset. The international visibility of some teams is yet to be improved. The recruitment of PhD students is still low.

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 unit carries out excellent translational science and has an excellent reputation.
It has a globally good level of scientific publications (> 2,500 papers, with 75% of them in the best journals of their disciplines and field of expertise and most of them in leading journals). Thirty-five CRCM researchers were or are members of 82 internationally recognised academies, scientific institutions and learned societies (Belgian Society for Extracellular Vesicles – board members –, senior member IUF, French society of Cancer – President of the Scientific Board –. Twenty-eight CRCM researchers were winners of 43 international, European or national scientific prizes and awards (Prize RAICES [Argentinian government], Grand Prix Ruban Rose de la Recherche 2020 [Cancer du Sein], Médaille de Bronze CNRS…).
All teams contribute to these productions and activity data, for all criteria, and there is a correlation between the number of permanent staff present in these teams and the numbers of activity products.
Most teams also have fruitful international collaborations (USA, Italy, Canada…).

Four International grants have been established (Indiana Univ, Fac Vet Suisse…), one ERC POC to one member (Team 11, 2018-21), and four other EU grants as coordinator (Starget-in-PANR-282036, FEDER_FIGHTCANCER, H2020-) and three as partner.
PMLingAML… The unit has raised a total of 3,414 M€ from international calls.

Weaknesses and risks linked to the context

The attractiveness of some teams still needs to be improved by increasing the number of invitations to international conferences as speakers and as members of the scientific committee or organising committees. Fifty-eight CRCM researchers (representing 72% of tenured researchers) have given a total of 377 lectures or have been invited to international conferences. This corresponds to less than one invitation per year per tenured researcher in average. Nineteen CRCM researchers (20% of tenured researchers) were involved in the organisation and/or seated on the scientific committees of a total of 49 international congresses. This relative low number is not in line with the high level of scientific production and excellence of the Unit.
The success rate in European projects and calls is to be improved.

There is a disparity in the quality and quantity of publications among the teams normalised by the number of the team's members.
The CRCM hosted only two visiting foreign scientists (Italy, USA) and less than 20% of foreign staff (students/postdocs).

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

Strengths and possibilities linked to the context

The unit has hosted 163 PhD students and 81 postdoctoral fellows. Early career researchers benefit from an environment and supervision of a high standard, providing good working conditions. They are given a welcome and orientation booklet, a welcome day is organised. Committees have been set up to organise the life of students and postdocs and representatives of these categories of researchers participate to the laboratory council. PhD students and postdocs are invited to participate in internal seminars.

There are 92 agents holding an HDR (half of the permanents), which enable the possibility to supervise more students. During the 2016–2021 period, nine young (5 CRCN and 4 MCU) and one senior (DR) external researchers were successfully recruited to the supervision bodies. Four ITA staff members were recruited in

parallel. The unit has been very successfully attracting new teams (3) in the period. In addition, the unit has put in place a proactive strategy to disseminate and encourage teams to optimise prevention in the field of Scientific Integrity, Ethics and Open Science: under the impetus of Inserm, the Labguru electronic laboratory notebook has been proposed and implemented; According to the production analysis data (Excel file attached), 54% of the documents are in Open Access, for a total of 2,173 documents, but this rate still increases significantly to 64% following the use of a specific CRCM query; the teams are progressively integrating the process of depositing their publications via the BioRxiv and HAL tools of the University of Aix-Marseille.

Weaknesses and risks linked to the context

The proportions of students (<2 students per HDR) and postdocs (<1 per HDR) remained low, for the period under evaluation.
The proportion of publications signed by PhD students with respect to the total production of the unit is very low (17%).
The involvement of PIs in master/PhD coordinating education programs is low.

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 very successfully attracting funds from different calls at the national level as well as industrial funding. From ANR calls (38 total,10 as coordinator), the unit has obtained a total amount of 6.8 M. A total of 14.2 M€ and 13.4 M€ were obtained from INCa (32 total, 16 as coordinator) and some foundations such as ARC Foundation, respectively. Finally, 3.4 M€ were raised from territorial communities (40 total and as coordinator) and by the Programme Investissements d'Avenir (PIA) ~ 9 M€. Three teams have the label FRM.

Weaknesses and risks linked to the context

Success rate as coordinator for national ANR calls is low

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

Strengths and possibilities linked to the context

The unit benefits from an excellent cutting-edge equipment and technological park, with highly skilled personnel. New spaces (Fight Cancer, IPC5, ex-cell therapy laboratory, …) will soon be available to rethink the centre's strategy and the organisation of existing spaces The CRCM, together with the IPC, has set up 18 technological platforms organized and coordinated in CoreTech, sharing a common Charter, occupying dedicated spaces and grouping together 10 M€ of equipment. Some platforms are certified by the IBiSA label (n=5), the AMU platform label (n=5) and three have the ISO9001 certification. The maintenance is shared by the IPC, in part, for about 400 K€ by the CRCM. They are open to industrial partners.

Weaknesses and risks linked to the context

The technological platforms are understaffed, risking a suboptimal functioning and loss of specific skills.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The scientific production has an excellent level, with shared publications within the unit. However, the level of publication is not uniform among teams.

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

Strengths and possibilities linked to the context

The unit showed an excellent level of scientific production: more than 75% of CRCM's scientific production is published between 2016 and 2021 in the best journals in their field of expertise.

The most representative papers of the CRCM are: Ann Oncol, 2xNature, Mol Cell, Blood.
An important number of joint publications among the unit's teams have been produced: Sci Adv, Nat Struct Mol Biol, PLOS genetics, Nat Commun.
More than 50% of publications are produced in the frame of international collaborations (Nature, Methods Mol. Biol. Nature Structural and Molecular Biology…).

Weaknesses and risks linked to the context
The level of publication is not uniform among the teams (normalised to the number of members).

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 significant number of publications (more than 2,500) has been obtained, and published mainly in Oncology. Haematology, Immunology, Transplantation, with a total of 280 Reviews.
20 % of the papers have been published in the best journals (Ann Oncol, 2xNature, Mol Cell, Blood), and more than 10% in link with industrial collaborations.

Weaknesses and risks linked to the context
There are several teams who only have one or two publications with another team of the unit.
The number (17%) of papers signed by students is low.
There is a disparity in the scientific production among teams (See Team reports).

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 number of Open access publications (54%, for a total of 2,173 documents) is very good and it is in an increasing phase. The data management plan is an asset.

The data produced are stored and backed up according to their origin, research data or patient data, either on the Storage/Backup part managed at the CRM level (DISC Platform), or on the Medical Data Storage part of the IPC on its certified health data component. These two components are currently being developed through the Equipex 4 D-OMICS program and a FEDER European funding to develop the IPC's data warehouse and to set up an organisation for regulated access to patient data in compliance with the RGPD and European directives.

Weaknesses and risks linked to the context
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

The unit has good and numerous interactions with companies involving both basic science and clinical trials. The unit produces numerous patents and helps the emergence of start-ups. Public outreach is exceptional. Thus, the assessment on this criterion is outstanding.

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

Strengths and possibilities linked to the context
The unit reached an excellent number (24) of R&D projects with industrial companies involving 6 teams, with 9 contracts for Team14.

This benefits from a regular participation of private companies (GSK, Innate Pharma, VECT-HORUS…) to team's research programmes.

It is also noted a strategic partnership contracts (Innate Pharma, BMS, Imcheck and others are being negotiated). In addition, CRCM host staff from private companies who strengthen its workforce on teams or platforms and consolidate the partnership, including researcher/engineers/technicians (n=15) and PhD students with CIFRE grants (n=5).
Twenty-four clinical trials involving industrial partners (Innate Pharma, GSK) and CRCM teams and/or platforms have been initiated

Weaknesses and risks linked to the context
The clinical activity of the medical doctors being very high, there is a risk of loss of clinical trials.
Twelve Teams have no RD contracts

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

Strengths and possibilities linked to the context
The CRCM has incubated four start-ups (Imcheck Therapeutics, Emergence Therapeutics) and hosts' companies (AB Science). The unit has reached an excellent number of patent applications (110) with nine licensed.

Weaknesses and risks linked to the context
The start-ups do not produce very specific products and this implies a risk of loss of competitiveness in this very very competitive domain.

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

Strengths and possibilities linked to the context
CRCM is active in disseminating scientific results. They participate in a series of events, such as 'Meeting of teachers and researchers' organised by the Academic General Directorate of Higher Education, with presentations and visits to the laboratories on the CRCM site.
CRCM members participate regularly to initiatives dedicated to the promotion of Science towards the youngest such as 'Apprentis Chercheurs', 'Fête de la Science', or DECLIC events (Dialogues Between Researchers and Students to engage them in the Construction of Knowledge.
The members of the CRCM are also involved in exchanges with patient associations and with the general public, such as 'Journée d'Information Patients' from the Rare Immuno-Haematological Diseases health network – MaRIH –, 'Researchers welcome patients' at the IPC – 2017 –, l'Université du Temps Libre – AMU, 2018 » , the PACA Cancéropôle 'General Public' meetings – Alcazar, 2019 –, 'Messenger RNA. What is it? A hope for the treatment of cancers?' – Marignane, 2021 –. Several members of the CRCM are very active on social networks – Twitter, LinkedIn – and other media in response to requests for interviews in various newspapers or television.

Weaknesses and risks linked to the context
The volume of outreach activities is unevenly shared within teams, and still low risking a loss of visibility within the local environment.

C – RECOMMENDATIONS TO THE UNIT

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

The unit is encouraged to keep reinforcing the link with the clinics and cancerology aspects, which are the main assets of the CRMC. In parallel, it is recommended to maintain and reinforce the interphase with the 3R teams by being attentive to create overlap among the recently created departments.
It is recommended to improve internal communication, especially in the following points:

i) the administrative staff should be able to communicate in English and
ii) the general meetings and corresponding minutes should be circulated in English;
iii) communication with ITA and within the teams should be improved.

The committee also recommends expanding the activities of the organoids platform to cancers other than pancreas as well as to modelling aspects on haematopoiesis, which would contribute to keeping the collaborations and projects with the APHM.

It is recommended to be attentive to guarantee the sustainability of the economic model of the platforms. The technological platforms should be strengthened in terms of manpower and national/international labels is recommended. The unit is encouraged to keep working and improve parity.

Recommendations regarding the Evaluation Area 2: Attractiveness

The number of invitations to international conferences and steering committees as well as participation in European projects and calls should be improved. More involvement of PIs in master/PhD coordinating education programs should increase attractiveness for students and is recommended. More participation in the organisation of conferences is desirable. A clear strategy on quality management should be set up.

Recommendations regarding Evaluation Area 3: Scientific Production

An effort must be made in terms of quality and quantity of joint publications among the teams
The teams are encouraged to increase the number of publications signed by the students.
A better traceability has to be reached.

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

More involvement in the development and strengthen of clinical trials should be reached.
Better targeting of products must be done.
The involvement of the unit's staff in debates in society should be increased.

TEAM-BY-TEAM ASSESSMENT

Team 1: Leuko/Stromal interactions in normal and pathological haematopoiesis

Name of the supervisor: Mr. Michel AURRAND-LIONS

THEMES OF THE TEAM

The team investigates the initiation and maintenance process of AML and B-leukaemia in the context of the dialogue with the bone marrow microenvironment. Data have highlighted the importance of the JAM-C integrin for stem cell maintenance. Molecular studies of the JAM-C identified a druggable domain of the protein. The team is particularly interested to decipher JAM-B/JAM-C expressions, interactions and roles in normal and pathological haematopoiesis and to investigate the molecular mechanisms allowing specific migration and adhesion of the different B cell subsets to their respective niches during normal or malignant B cell differentiation. The description of specific bone marrow specialised domains for healthy pro-B cells have been achieved. Experiments are mainly conducted in preclinical models.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The main recommendation of the previous evaluation was to improve the rate and impact of the team's publications that would allow increasing their international recognition. Thanks to a strong expertise and the development of unique tools to study cell adhesion in vivo, the team implemented a lot of collaborations with internationally renowned teams. Following past recommendations, the team has globally increased the level of publication over the period for which members of the team have a leadership position (PDC) (Cancer Research, Blood Advances, PLOS Genetics, Cell Reports…). However, their best and outstanding publication is a co-authoring in Immunity journal outside the team's field.

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	1
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	1
Research supporting personnel (PAR)	2
Subtotal permanent personnel in active employment	**5**
Non-permanent teacher researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	1
Post-docs	0
PhD Students	3
Subtotal non-permanent personnel	4
Total	**9**

EVALUATION

Overall assessment of the team

The team has very good to excellent contributions (Cancer Res. PLOS Genet). Within their scientific field of the haematopoietic niche focused on the function of the JAMC/JAMB in HSC aging, myeloid tumour initiation and treatment escape. It is scientifically very strong and productive with a very good attractiveness and a deep investment in the setting of several CRCM platforms. The training through research activities of this team is excellent as well as interactions with the non-academic world. The overall scientific output of the team is very good to excellent.

Strengths and possibilities linked to the context

Based on their expertise in immunology, haematology and ligand/receptor cell biology, the main research program of the team is the study of the functional interaction between stromal cells and leukocytes in bone marrow and of the role played by those interactions in normal and pathological haematopoiesis. From 2016 to 2021, the team was organized in two groups developing two complementary axes of research: the study of junctional adhesion molecules in Leuko/Stromal interactions in bone marrow and the deciphering of regulatory mechanisms of normal and pathological B cell development/survival in stromal cell niches. During this period, the team made a significant contribution in the field and demonstrated that:

i) the haematopoietic stem cell adhesion molecule JAM-C is a marker of poor disease outcomes in AML;
ii) the C-terminal part of JAM-C interacts with the Golgi reassembly protein GRASP55 via a druggable PDZ domain interaction;
iii) the interaction is necessary for the function of JAM-C in male germ line cells and does not play a role in haematopoiesis, and iv) that healthy pro-B cells are localized in specialised niches of the bone marrow.

The team has published 26 scientific articles including twelve original articles and reviews as first, last or corresponding author by a team member (Cancer Research, Blood Advances, PLOS Genetics, Cell Reports).
Four PhDs have defended over the period (for 2 HDR in the team) and all PhD students and postdoctoral fellows (2 hosted during the mandate) published at least one article as first author.
The team acquired a national and international recognition through its works on the JAM-C protein and haematopoiesis and involvement of team members in key national networks (the PI is a member of the scientific council of CHO and SFH and the team is a member of GDR-CNRS3697 Micronit).
Due to this strong expertise and unique tools to study cells/adhesion in vivo, the team has developed a lot of collaborations even outside the haematologic field and with internationally renowned teams (co-authoring a publication in Immunity).
Over the period, the team had a strong involvement in technological developments and became a leader in the single-cell technology allowing original and efficient translational and transdisciplinary approaches. This also leads to deposit of three inventions disclosure. The team leader is involved in the management of two platforms (the experimental histopathology platform).
A clear strength of the team is its ability to raise funds (most of them are from national grants). Indeed, several national contracts have been obtained as PI (ANR, 2 INCa, BPI), two from local institutions (Cancéropôle, Conseil régional PACA) and more than ten from charities (LNCC, ARC, *Fondation de France*). The team has also been awarded with contracts with private companies to develop new imaging tools (First Light Imaging to develop CMOS camera) and to fund a PhD student (Innate Pharma) or an engineer (MiMabs).

Weaknesses and Risks linked to the context

The manpower of the team is impaired by the departure of one PI mainly involved in axis 2 and the absence of postdocs which could impact the development of the projects. Therefore, the team face a limited number of permanent researchers (2) since at least two years. As a consequence, the PI indicated heavy-duty from team leadership but also by the charge of platform management. The team then encounter difficulties to maintain and propagate specific knowledge and skills built over the years and are recognised for. Though the capacity for funding research is good, the team has no European or international funding allowing them to be more attractive to recruit international postdocs. Though the team has established collaborations with internationally recognised teams such as Christoph Scheiermann and David Lyons teams, these collaborations concern research outside the field of the team and members are rarely invited to speak at international conferences. The team has not been involved in organising national or international meetings or conferences.

RECOMMENDATIONS TO THE TEAM

The team should put in place a strategy to attract and recruit postdoc eligible for CRCN recruitment for long-term strategy of the team. The international visibility of the team can be increased, e.g. by better representation at international meetings. Due to the lack of a PI involved in axis 2, it is recommended that the team limits its research axes and strengthens the fundamental research part. As the manpower of the team is limited particularly in researchers, the leader of the team should limit his involvement in platform management to dedicate more time to science.

Team 2: Molecular Mechanisms of Tumour Cell Migration

Name of the supervisor: Mr. Ali BADACHE

THEMES OF THE TEAM

The team explores the impact of cytoskeleton-associated supramolecular complexes on cell properties (morphogenesis, contractility, biomechanics). The team identifies and validates supramolecular complexes as functional units ('molecular machines'); most participate into biological processes involved in the oncogenic process. This research builds a continuum from cell biology (subcellular scale) to interactomics (macromolecular scale) to structural biology (molecular and atomic scale).

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Based on the 2017 HCERES evaluation, INSERM did not renew the team headed by A. Badache.
No oral presentation. Review based on the scientific document only.

WORKFORCE OF THE TEAM

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

EVALUATION

Overall assessment of the team

A. Badache left the CRCM at the end of 2021 to join the Centre de Génétique Médicale of Marseille.

Strengths and possibilities linked to the context

The team publishes in high quality/impact research journals, and has made the choice of publishing less, but comprehensive studies. The team targets journals highly read in its community, managed by active scientists (J Cell Biol) or learned societies (PNAS; J Cell Sci), favouring open science (PNAS, J Cell Biol, J. Cell Sci, Cells, Sci

Rep). With only 3.5 permanent members in the team over the last five-year period, the group managed to publish twelve articles, which is a very good achievement. The publications as last authors include: PNAS 2017 (A. Badache), Sci Rep 2020 (A. Badache), J Cell Biol 2021 (A. Badache) and J Cell Sci 2022 (P. Verdier-Pinard). The team has an internationally recognised expertise in the field of *in vitro* assembly of microtubules and actin filaments, leading to co-publications with partners of high levels (Bruce Goode: Juanes et al. J Cell Biol 2017; Juanes et al., J Cell Biol 2019; Eva Anton: Nakagawa et al., Neuron, 2019; Kuzmic et al., bioRxiv 2021).

Weaknesses and risks linked to the context

The weaknesses of the team in terms of publication and manpower were assessed during the last mandate and led to its departure from the CRCM

RECOMMENDATIONS TO THE TEAM

If still applicable (as the team moved out): put in place a strategy to recruit postdoc eligible for INSERM/CNRS recruitment for long-term strategy of the team.

Team 3: Machine Learning for Precision Oncology and Drug Design

Name of the supervisor: Mr. Pedro BALLESTER

THEMES OF THE TEAM

The team research focuses on the development and application of computational methods to predict and analyse the modulation of protein and cell function by small organic molecules. Based on relevant data, the team is generating predictive models using machine learning (AI for drug discovery). The team strategy considers integrating feature selection with machine learning algorithms to build classifiers that use only a much smaller subset of features (the most discriminating ones). They also address the challenge of how to best interpret a prediction based on the selected genetic alterations to explain why a specific tumour is sensitive or resistant to treatment.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The main recommendations of the previous evaluation were to improve the impact of the team's publications and to synergize with CRCM chemists and scientists as well as with other research centres in order to create unique skills to the CRCM/IPC and avoid redundancy in the developing tools of modelling.
Thanks to a strong expertise and the design of unique tools for the development and application of computational methods to predict and analyse the modulation of protein and cell function by small organic molecules, the team has succeeded in both implementing a lot of collaborations with internationally renowned teams and globally increased the level of publication over the period. However, the integration within the CRCM does not seem to have been sufficient to maintain the activity of this team in the CRCM as the PI decided not to renew his team for the next contract and moved his research activities to the UK.

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	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)	0
Subtotal permanent personnel in active employment	**1**
Non-permanent teacher researchers, researchers and associates	5
Non-permanent research supporting personnel (PAR)	1
Post-docs	0
PhD Students	0
Subtotal non-permanent personnel	**6**
Total	**7**

EVALUATION

Overall assessment of the team

NA

Strengths and possibilities linked to the context

Over the period the team has been highly productive and the quality of the publications is recognised by the high number of citations for research in this area. The vast majority of publications, including the most cited, are led by the team leader showing that this is mostly the team productivity even if the network of collaboration at international level is of importance. The team has been developing major tools with several software that have been patented and licensed by several pharmaceutical companies. The team was a pioneer in the investigation of the suitability of the largest dataset of drug synergy measurements on cancer cell lines to predict the synergies of other drug combinations.
This team has been instrumental for introducing translational research in the CRCM (AI for drug design and AI for precision oncology). Local integration has started as attested by in in-house translational and clinical collaborations. This team has raised a sufficient funding for their projects (including 1ANR as PI and 1 ANR tremplin/ERC applicants, and as participant 1ANR, 1ITMO GGB, one international contract and 2 from associations).
This team has been involved in several meeting organisations and the PI is part of the editorial committees of seven different journals. The interactions with non-academic partners are excellent and very good with social-economic actors.
The team gathers scientists of various nationalities and training backgrounds that strongly contribute to the originality of the scientific production.

Weaknesses and risks linked to the context

The manpower of the team is limited to the sole PI and during the period it was difficult to recruit even PhD students or postdocs. Now the team has reached a sufficient number of docs and postdocs but still no permanent researchers. This situation has seriously limited the growth of this team, as the PI was the only member of this team who can write grant proposals and supervise other members. This will impact the long-term evolution of the team and integration in the CRCM.
The policy for the development of products devoted to the socio-economic world is relatively weak regarding the originality and translational potential of the scientific project of the team.

RECOMMENDATIONS TO THE TEAM

If still applicable (as the team is currently in the process of moving out to the UK in 10/2022):
Put in place a strategy to recruit postdoc eligible for CRCM recruitment for long-term strategy of the team. Reinforce the fundamental research axis.

Team 4: Antibody Therapeutics and Immuno-targeting

Name of the supervisor: Mr. Patrick CHAMES

THEMES OF THE TEAM

The main interest of the team is to generate new molecules from engineered nanobodies to use for cancer therapy via their ability to modulate the anti-tumour immune response through the recruitment and activation of innate immune cells such as NK cells. By engineered nanobodies conjugated with fluorescent dyes or sensors, the team proposes to use them for cancer diagnosis.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The committee of experts recommended to the team:

1) to focus on a limited number of targets and to perform a detailed proof of concept of feasibility and activity and
2) to implement collaborations with groups that are expert in immune checkpoint inhibitors and/or search for the required expertise.

During the last period, the team developed several collaborations with recognised experts allowing them to go further in the investigation of selected targets. Although, most collaborations led to collaborative publications the number of targets and consequently the number of projects remain large for a small team.

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	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	**4**
Non-permanent teacher researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	3
Post-docs	0
PhD Students	4
Subtotal non-permanent personnel	**7**
Total	**11**

EVALUATION

Overall assessment of the team

The research performed by the team is excellent with very good publications (Nat Commun., Sci. Rep.) in the field of nanobodies and their use in cancer therapies or imaging. The team is recognised at the international level and was successful in grant funding, its attractiveness is excellent. Due to the potential of nanobodies in therapeutic and imaging applications, the team has an outstanding level in valorisation. The global assessment of this team is excellent.

Strengths and possibilities linked to the context

The team has a solid expertise in the generation and engineering of nanobodies and uses this expertise for the development of innovative cancer imaging and immunotherapy. The team is pioneered in France and developed an internationally recognised expertise in this field.
The team has published fifteen scientific articles including thirteen original articles and two reviews as first, last or corresponding author in general journals (PNAS, 2021 and Nat Commun, 2017) or specialised journals (Oncoimmunology, 2022 and 2021; Front Immunol, 2019; Front Pharmacol. 2020 and recently Nat Chem Biol).
The team leader was the editor of the book 'Antibody engineering: Methods and protocols, Third edition. Springer Verlag (2018).' He is associate editor for Frontiers in Immunology, section Cancer Immunity and Immunotherapy and in the editorial board of Antibodies (MDPI).
Team members have been invited several times to present their works (GSO Canceropole – 2018 –, Antibody engineering and therapeutics – 2017 –, 40th Congress of Spanish Society of Immunology – 2016 –, University of Science and Technology, Wuhan – 2016).
The team is deeply involved in the training of students. Eight PhD theses were defended in the team during the period and four of them published their results in peer review journals (OncoImmunology, Antibodies, Front Immunol, Methods Mol Bio, etc.) l and two others have not yet been published for IP protection reasons due to a collaboration with industries (Cisbio bioassays and VectHorus) but they are involved in a patent as co-inventors.
Team members participated in various scientific committees and performed several expertise for various institutions, including la *Ligue nationale contre le cancer*, FWO (Flanders Research Foundation), la KWF Kankerbestrijding (DutchCancer Society), European Research Council, Cancéropôle Grand Sud Ouest, Fonds de la Recherche Scientifique (FNRS) belge.
The team leader developed a platform to generate and engineer nanobodies. This activity allowed the team to initiate and develop collaborations with internationally renowned groups in their fields of expertise. Moreover, due to the potential of engineered nanobodies in therapeutic and imaging applications, the team established several collaborations with local and national biotech companies (Innate Pharma, Sanofi) and could benefit from funding from tech transfer offices such as Inserm transfer and SATT Sud Est. The team filed several patents (7 patents, 1 licensed with Cisbio).
The team has a very good capacity to fund its projects through mainly national contracts from ANR, INSERM Transfert and Plan Cancer as PI; from charities (INCA, ARC as PI) and from local grants (Gefluc, Canceropole PACA, SATT Sud Est). Most contracts are obtained as PI.
The PI of the team is involved in teaching (40 h/year in Master 2 Immunology pro, Aix Marseille University).

Weaknesses and risks linked to the context

The team has no European or international funding that would allow them to be more attractive for international postdocs and to recruit them.
Although the team and its PI are well recognised in the nanobody field, they have not been involved in the organisation of national or international meetings.

RECOMMENDATIONS TO THE TEAM

As the manpower of the team is limited, the team should put in place a strategy to attract postdocs eligible for CRCN recruitment.
The team should initiate more mechanistic studies that may be published in prestigious journals.
It is also recommended to favour collaborations with other CRCM teams which could bring their expertise in immune checkpoint therapies, preclinical models and clinical trials.

Team 5: Cell polarity, Signalling and Cancer

Name of the supervisor: Mr. Jean-Paul BORG

THEMES OF THE TEAM

The team studies the molecular events that alter the morphology and function of tumour cells and give them the ability to invade distant organs. The core activity and main contributions of the team are related to protein networks involved in cell migration and invasiveness (scaffolding proteins LAP involved in epithelial cell polarity and their contribution to neoplastic processes, as to chemo- and radio resistance and metastatic dissemination) with a special focus on the role and alterations of regulators of cell polarity and of the non-canonical Wnt signalling in physiological processes and cancers (triple negative breast cancer, lung). Targeting components of non-canonical Wnt pathway is a new and promising topic still very much open with opportunities for therapeutic developments in cancer and discoveries.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Among the recommendations of the previous report, it had been suggested that the international visibility of the team could be increased. Co-publications with partners of the highest international level attest from the team's visibility.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	5
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	0
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)	3
Subtotal permanent personnel in active employment	**11**
Non-permanent teacher researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	0
Post-docs	1
PhD Students	2
Subtotal non-permanent personnel	3
Total	**14**

EVALUATION

Overall assessment of the team

The team leader who is also the director of the CRCM has an outstanding activity in time-consuming collective duties and responsibilities. The team has an excellent scientific activity and production. Most projects are well funded and led to the development of fruitful internal and external collaborations and generations of reagents of high value. The tight link of the team in two platforms is a true asset. Attractiveness has been excellent over the evaluation term and the announced arrival of several additional high-profile senior scientists that have the potential to be co-team leader or/and project leader is seen as an asset for the future development of this team. The team leader has an outstanding activity in the development of collaborations with socio-economic world and in general, stands out by the quality of its non-academic interactions.

Strengths and possibilities linked to the context

The team leader (IUF, PUPH pharmacy) has an outstanding personality and activity. He is also director of the CRCM and strongly involved in other time-consuming collective duties and responsibilities, at the local level (vice Dean of the Faculty of Pharmacy, scientific director of IPC cancer hospital, Institute of Cancer and immunology), and at regional and national levels. Hence, the team leader and clinicians associated with the team are/have been actively involved in the writing of recommendations and strategic plans of Inserm, INCa, UNICANCER, Plan Cancer Region PACA, Pôle de compétitivité Eurobiomed, as well as in the implementation of standard procedures at Institute Paoli Calmettes.

The scientific production is excellent to outstanding (> 41 publications between 2016-21), as ASC Chem Biol 2022, J. Cell Sci, Oncogene 2020, PNAS 2020, Br. J Cancer 2019, Proteomics, Stem Cell Reports 2018, Trends in Cancer 2017, Nat. Commun 2016, Developmental Cell 2016; J. Immunology 2016); most are signed in major position by a team member (PDC) without considering medical publications of the clinicians associated with the team, original articles or reviews, in peer-reviewed journals, of which> 90% are in A-ranked journals, and 100% published in open access and/or in free access in HAL (AMU-Inserm).

Due to its attractiveness, the team was joined by two new university assistants – professor (MCF, Pharma & Sciences Faculty), an engineer of Research (IR) from the IPC, six postdoctoral fellows and eight PhD students.

During the visit, the team leader announced to the evaluation committee the upcoming arrival at CRCM and the merger with the team of a high-level external research group previously located in another CNRS institute of Marseille. The venue of this group of researchers, headed by an excellent scientist that has the potential to be a co-leader of research programs in the team is seen as an asset for its future development. This will undoubtedly help to supervise research and will enhance funding activities of the team.

Current team members took part into numerous conferences (35 invitations, including international meetings in China, Denmark) and received three scientific prizes.

The team has developed solid internal and external collaborations (academic and non-academic) at the national (for instance with Dr. A. Le Bivic — IBDM – for a project on cancer stem cell and mechano-transduction) and international (for instance with Pr. I. Macara – University of Tennessee – and T. Johansen – University of Tromsø, Norway – for theVangl2 projects; with the Pr. Stephane Angers – University of Toronto, Canada – for the MINK1-PRICKLE1 project; with the Pr. K. Strømgaard – University of Copenhagen, Denmark – for PDZ interactions in cancer and neurons) level.

Seven PhD defences were reported and six postdoctoral fellows were hosted. Most postdocs and PhD students have published at least one paper in leading position (Stem Cell Reports, J of Cell Science…).

Most projects include high-profile basic/fundamental and translational approaches, thanks to a broad use of the institute's technical platforms and to a privileged access to patient samples facilitated by the presence in the team of the Head of the Medical Oncology Department of IPC, an undeniable asset for this team and an example of reasonably successful and true clinician-researcher collaboration.

The position of leader in its field and this clear link with the clinic has also been the source of fruitful collaborations with biotechs (AB Sciences, Synsight Inc), and participation to National and European funded networks (H2020 ITN…). There is also a tight link of the team with two platforms (proteomics – MaP, IBiSA/AMU platform – led by the team leader – an engineer in the team is responsible for the transgenic platform of CRCM – , an asset for the team's projects – multidisciplinary technic, procedures and approaches – and collaborations.

All research programs of the team benefit of excellent funding of various magnitudes – including PLBIO, AVIESAN and labelisation by the *Ligue nationale contre le cancer* – mainly obtained in the context of competitive national calls – 5 M€ in total over the evaluation term – . Noticeably, the team has been continuously certified and funded by the French *Ligue contre le Cancer* over the evaluated period.

The team has an outstanding activity in the development of collaborations with socio-economic world and in general, stands out by the quality of its non-academic interactions.

Weaknesses and risks linked to the context

The very strong and remarkable involvement of the team leader in collective activities outside the team is gradually taking place to the detriment of the activity in his own team, which is reflected in a recent decline in the level of publication of the team in high audience journals – usual symptoms of Institute directors in France … whose scientific activity is not sufficiently 'protected' by the community –, with the risk of seeing the team's appeal, currently excellent, weaken in the medium/long term – a warning signal is the number of PhD students that is currently low –.

It should be noticed that the publication record of some permanent researchers of the team could be better, and while national academic and non-academic funding are excellent, European funding could be improved. Only four HDR are represented in the team with eight PI.

RECOMMENDATIONS TO THE TEAM

The team has developed tools of high value – inhibitors, antibodies, preclinical models – that will probably continue to be the source for additional and future collaborations, but which in this prospect could be better secured from the point of view of the intellectual property.

During the visit, the team leader announced to the evaluation committee the upcoming arrival in the team of a high-level external research group headed by an excellent scientist who is currently leading a CNRS team in another institute. The review panel believes this merger is an asset for the evolution of the team and its day-to-day scientific co-supervision of laboratory activities but highly encourages the implementation of clear operating rules for this new organisation and recommends the identification of points of convergence of the respective research programs and of actions to develop them as priorities.

Team 6: Integrative Structural and Chemical Biology

Name of the supervisor: Mr. Yves COLLETTE and Mr. Xavier MORELLI

THEMES OF THE TEAM

The team develops a large panel of approaches for designing new molecules targeting protein-protein interactions which represents an alternative and a very large unexplored reservoir for drug development in oncology. The team not only develops technological tools in bioinformatics – database and virtual screening – and in cell biology – phenotypic screening – but also focuses on three main applications on validated drug targets, the development of inhibitors of bromo-domain for applications in breast cancer, inhibitors of deoxycytidine kinase for applications in leukaemia and inhibitors of immune checkpoints in myeloid cells with applications in oncology but also in virology.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The excellent reputation and visibility as well as its excellent financial support were already highlighted in the previous report. Following the recommendations of the previous report, the team implemented during the evaluation period – 2016–2021 –, in relation with the MRCC – Metastatic Renal Cell Carcinoma – platforms, new developments of phenotypic screens for the identification of relevant physio-pathological mechanisms to be screened with the original chemical database they have built.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	2
Senior scientist – Directeur de recherche, DR – and associate	2
Scientist – Chargé de recherche, CR – and associate	4
Other scientists – Chercheurs des EPIC et autres organismes, fondations ou entreprises privées –	1
Research supporting personnel – PAR –	1
Subtotal permanent personnel in active employment	**10**
Non-permanent teacher researchers, researchers and associates	0
Non-permanent research supporting personnel – PAR –	3
Post-docs	5
PhD Students	12
Subtotal non-permanent personnel	**20**
Total	**30**

EVALUATION

Overall assessment of the team

The research performed by the group is excellent to outstanding with a remarkable scientific production in the field of drug design applied to protein-protein targets in cancer. The attractiveness of this team and its interactions with the non-academic world are outstanding. In particular, the group was successful in grant funding and was remarkably active in establishing collaboration within the CRCM and valorising its findings with patents and industrial partnerships. The global assessment of the team is outstanding.

Strengths and possibilities linked to the context

The team is currently composed of thirteen permanents and ten temporary staff, including four PhD students and four postdoctoral fellows. It integrates researchers with a wide range of skills in chemo-informatics, structural biology, biophysics, chemo-biology and preclinical studies who cooperate with a collegial organisation. During the period 2016–2021, the team has been attractive and has been strengthened by the arrival of four new PIs, which lead to the creation of a new emerging group, led by Eddy Pasquier – bronze medal of the CNRS commission 28 in 2021 –.

During the period, the team published 92 papers including high impact journals: as PI in ACS Chem Biol, Nature Commun; PLOS Genet., and as collaborators in Cancer Discovery, Trends in Cancer, NAR… More than 30 papers are signed as first, last or corresponding author by members of the team. These papers also include collaborations with internationally recognised collaborators. All researchers contribute to transversal projects of the team as attested by the fact that the publication list presents a good balance between the different PI and students from all the team. The national and international visibility of the team is obvious as attested by 31 invited conferences of all PI of the team – 6th biannual International Metronomic and Anti-angiogenic Meeting, Conference at the international conference on 'Big data analyses in evolutionary biology', 17th annual Drug Discovery Chemistry conference, … —.

Attractiveness of the team is also revealed by the arrival of a CRCN member – 2016 –; a MCU in 2017; a US researcher with his own funding – RO1-NIH – and the sabbatical of a visiting professor from British Columbia.

The team is particularly well integrated in the CRCM and collaborates with many other teams of the institute.

In addition, the team highly succeed in finding funding during the period – reaching around 1.8M€ – from various public and charities sources – including two ANR, INCa, SATT Sud-Est/Canceropôle PACA 'Maturation Grant, ARC –.

It was remarkably active in establishing interactions with industrials – ABScience, ESAI, PSTx, CisBio, Hybrigenics – and developing technological resources including databases, and five patents during the period 2016–2021.

The team is also highly involved in training, it includes six HDR and eight PhD defence were supported; four postdocs were hosted. Several members are also active in science spreading in for school pupils – DECLIC events, REACT-4kids –.

Weaknesses and risks linked to the context

Due to multiple solicitation, the team could disperse its forces in too many projects.

RECOMMENDATIONS TO THE TEAM

The joining of complementary expertise of chemists with cell biology as well as bioinformatics and structural biology has been a success with the achievement of successful pilot projects. The team is encouraged to continue to extend its drug discovery technology to other targets, but also to be careful not to lose focus. In particular, the team is encouraged to select targets for which there is a strong expertise at the CRCM.

Team 7: Signalling, Haematopoiesis and Mechanism of Oncogenesis

Name of the supervisor: Mr. Paulo DE SEPULVEDA and Mr. Patrice DUBREUIL

THEMES OF THE TEAM

The team has a strong focus on haematopoiesis with a particular emphasis on c-Kit driven oncogenes, signalling, haematopoiesis, tyrosine kinases, epigenetics, and cancer. The team identified mechanisms, transduction pathways and protein effectors affected by genetic alterations of c-Kit tyrosine kinase receptors in several pathologies such as blood disorders, mastocytosis, gastrointestinal tumours and melanomas. Ultimately the goal of the team is to use its expertise and tools to study other receptors important in onco-haematology such as FLT3. A more recent research theme is emerging which focused on the metabolic underpinnings underlying systemic mastocytosis aggressiveness; these studies could also lead to therapeutic developments.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Among the recommendations of the previous report, it had been suggested that the team develops a strong network of collaborations, both inside and outside of IPC, to perform translational projects on AML.
The team developed two international collaborations on haematological malignancies with JD Griffin – Dana-Farber Cancer Institute – and N. Gray, Harvard Medical School). They have a publication in common (Br J. Haematol, 2019). It was also suggested that the team identifies new alternative original therapeutic agents or targets as it was done for the masitinib, now in advanced clinical trials. The team maintains a collaboration with AB Science Company to identify new substrates/new pathways associated with the c-Kit oncogenic signalling.

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	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)	1
Subtotal permanent personnel in active employment	**5**
Non-permanent teacher researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	3
Post-docs	1
PhD Students	4
Subtotal non-permanent personnel	**8**
Total	**13**

EVALUATION

Overall assessment of the team

The global scientific output of the team is excellent. The team contributes at high levels to the development of both basic and translational analyses on a rare disease, the mastocytosis, and has in parallel developed important studies on the contribution of mutant forms of tyrosine kinases as c-Kit, in haematopoietic and other human malignant diseases. The scientific production of the team is excellent, and also includes three patents recently submitted. The attractiveness of the team is very good (recruitment of several PhD students and postdocs in the team). Due to the involvement of AB Science in collaborative projects, valorisation of the team is excellent.

Strengths and possibilities linked to the context

The team has an excellent level of publication (35) including Blood, PLOS One, Nat Commun, JCI. Notably, the team produced excellent results in the field of mastocytosis, a rare disease leading to the discovery of very original observations on a tyrosine kinase inhibitor (Nat Comm. 2017). They also demonstrated the implication of FES kinases in a human pathology in AML (JCI 2017).
PIs are members of the national Mast cell national consortia (AFFIRM, CEREMAST) and the European mastocytosis network (ECNM). The team is the reference centre for genotyping of mastocytosis patient samples in France and manages the national database of cryopreserved primary sample resources.
The team has a good capacity to fund its projects: INCa PLBIO, Ligue LNCC and three from charities (3 ARC, Fondation de France); Emergence Canceropole; two Prématuration Cancéropole
The projects of the team are interdisciplinary involving life science, chemistry, structural biology, metabolomic, and bioinformatics and rely on a mix of basic and preclinical research based on the development of original preclinical models (AML-PDX model and mast cell leukaemia models).
Members initiated international collaborations with Dr. John M. Asara (Harvard Medical School, BIDMC), Dr. Alberto Orfao (Salamanca, Spanish reference centre for mastocytosis), and Dr. JC Marine (VIB UK Leuven). They also collaborate with hospital clinical departments for clinical studies (IPC and Necker Hospital, Paris) and has joined publications.
The team developed a long-time collaboration with the AB Science company (one of the team leaders is cofounder of AB Science Company) (2 permanent staff from AB Science work in the lab).
The team is involved in the training of students. Three PhD theses were defended in the team during the evaluated period and three are ongoing. There is a good ability to attract postdocs (national and international). Three postdocs were in the team over the period and one is still present.
In terms of valorisation, the team filed three patents during the period, two in 2021 and one in January 2022.
One of the team leaders has an editorial activity (Cancers).
Members were invited to international meetings (Int Symposium on models of skin cancer; World cancer congress).

Weaknesses and risks linked to the context

The team has little interaction with other CRCM's groups.
Members develop a lot of different research projects, which may be difficult to sustain, due to the upcoming retirement of two permanent staff (1 PI, 1 technician).
The number of postdocs currently in the team is low.

RECOMMENDATIONS TO THE TEAM

The team should anticipate the retirement of the PI who is co-founder and head of the AB Science scientific company and the consequence of the collaboration with this company, the access to molecules, and the future of AB Science staff working in the team and especially on the future of his projects.
The team should pursue the development of both basic and translational studies on mastocytosis and maintain the visibility of this team on the topic.
The team should strengthen interactions with CRCM teams or IPC department, particularly on AML projects.
An implementation of a strategy to attract and recruit new postdocs is recommended.

Team 8: Epigenetic factors in haematopoiesis

Name of the supervisor: Mrs. Estelle DUPREZ

THEMES OF THE TEAM

The team aim to decipher the transcriptional networks involved in the regulation of proliferation versus differentiation of normal or pathological haematopoietic cells (HSC) with a focus on the stem cell compartment. Members are investigating epigenetic mechanisms in normal haematopoiesis and their deregulation upon aging and in leukaemia. In collaboration with clinicians of the Paoli-Calmettes Institute, the team also develops translational research programs on AML using epigenomics-based information to improve AML treatments and care. The team is developing transdisciplinary collaborations with mathematicians and bioinformaticians in the context of omics analysis and modelling.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The main recommendation of the previous evaluation was to improve the size of the team, its involvement in large and more competitive grants and to focus projects on internal strengths to increase international recognition. Thanks to the multidisciplinary expertise of the team on epigenetic regulation of HSC during aging and leukaemia, and to the development of new mathematical tools applied to this theme, the team has achieved an excellent publication record. Nevertheless, their international recognition remained below what they could pretend with only four international invited communication of the PI in modest meetings. They have recently joined an EU network group on AML involving fifteen teams.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	1
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	0
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	3
Subtotal permanent personnel in active employment	**5**
Non-permanent teacher researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	4
Post-docs	1
PhD Students	0
Subtotal non-permanent personnel	**5**
Total	**10**

EVALUATION

Overall assessment of the team

The research and scientific production are excellent to outstanding with a very constant and regular production output. This high level of scientific activity is competitive and has been at the fore front in the field of the epigenetic control of leukemogenesis and of stem cell aging. The team's reputation and visibility are excellent at the regional and national level but could easily be improved at the international level. The training through the research activities of this team is excellent. The interaction with the non-academic world has been limited.

Strengths and possibilities linked to the context

Despite the small size, the team has delivered constant excellent quality results in their field and published regularly, including seven article and one review (Blood 2021) as PI, in the best journals, including in the most visible one (Blood 2022, 2021, 2016; NAR 2018, 2019, PNAS 2018 as main examples). Altogether, this record confirmed that the team as a whole has reached an excellent level of expertise and has engaged fruitful transdisciplinary collaborations, in particular with mathematicians and bioinformaticians, on the epigenetic and transcriptomic aspects of haematology. Noticeably, through these associations the team largely invested over the period in a successful move to single cells and multi-omics analyses that resulted in a growing national and international recognition in this very competitive field, as illustrated by invitations to international meetings (Fourth international conference on stem cells, development & cancer, Lyon 2022, ARCH 2nd meeting Roma, Italy; Epigenetic regulation, three invited talks in Japan 2017 – Chiba University, Kyoto University, Kumamoto University.).
This work also led to an excellent activity of valorisation and funding as illustrated by the filing of three inventions disclosure and one patent, the certification of the team by the 'Ligue nationale contre le Cancer', the participation to an EU project and the regular success in obtaining competitive grants at local and national levels as PI (3 from governmental agencies as INCa PRTK, Plan Cancer, …); Two from local authorities and seven from charities (ARC, GEFLUC, etc..).
The PI has been involved in the organisation of local scientific events and is an active member of French scientific societies and networks in the field. The team had four doctoral students that defended their PhD during the period and has trained two Postdocs.

Weaknesses and risks linked to the context

The manpower of the team was limited during the evaluated period, especially in terms of permanent researchers, a situation that has limited the potential for students' formation and slowed down project developments. Noticeably, this weakness will be corrected in 2023 with the arrival in the team of three additional permanent researchers for the new contract (1DR2, 1CRCN and 1 MCU-PH), also a good sign that reflects the attractiveness of the team.
The team had limited interactions (meaning no industrial contracts or interactions with the general public, non-academic and socio-economic world over the period. The team should be watchful in maintaining its sustainable originality and competitiveness.

RECOMMENDATIONS TO THE TEAM

Considering the crowded and highly competitive field of research at the international level, the panel encourage the team to identify a 'niche' and to focus on a limited set of projects for the future. Such projects should reinforce connections with clinicians of the IPC, a true asset as compared to teams located in most academic institutes. The team should improve its interactions with non-academic partners to better value team's findings.
Considering the recognised know-how of the team in the field, the committee encourages the team to apply for international grants (including on a collaborative basis) to obtain more return from their effort. With appropriate communication, the review committee believes that the cutting-edge questions currently addressed should improve the team participation at high-profile meetings, international communication and attractiveness. For that, the team should take advantage of its participation in an EU-ETN network to extend its visibility in Europe and increase this international recognition and to attract self-funded postdoctoral fellows.
To ensure preservation of competitiveness of the team during the next contract, a strategy defined collectively should accompany new senior researcher arrivals scheduled in 2023 to maintain team cohesion and ensure synergies between the sub-projects.
Look, together with other CRCM teams, for a more stable organisation of bioinformatics support (at the level of the unit and on the long term). The interactions with the non-academic world could be improved.

Team 9: Structure-Specific Endonucleases and Genome Stability

Name of the supervisor: Mr. Pierre-Henri GAILLARD

THEMES OF THE TEAM

The team focuses on the investigation of mechanisms that contributes to the genome stability with a focus on the control of the structure-specific endonuclease. The understanding of the different modes of regulation of these endonucleases is a major challenge in the field and a speciality of the team for several years with a special focus on the SLX4 endonuclease.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The excellent quality of the team was highlighted and the committee recommended a full support to this team by the CRCM. The team was encouraged to put more efforts in outreach activities and teaching and interactions with economic applications. In this line, Gaillard team initiated a collaboration with team 6 of Colette/Morelli to screen small molecules targeting interaction of the endonuclease SLX4 with different partners for applications in cancer therapies. The team also initiated collaborations with two teams from Gustave Roussy Institute with translational projects and applications in metastatic breast cancer.

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	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)	1
Subtotal permanent personnel in active employment	**5**
Non-permanent teacher researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	1
Post-docs	1
PhD Students	0
Subtotal non-permanent personnel	**2**
Total	**7**

EVALUATION

Overall assessment of the team

The research performed by the group is excellent with remarkable publications of the team as PI in the field of genome stability (including 1 Mol Cell 2019 in collaboration, 1 NSMB 2020 as first and last author). The team is recognised at the international level and was successful in grant funding (INCa PLBIO and Equipe FRM), its attractiveness is excellent. The global assessment of this team is excellent.

Strengths and possibilities linked to the context

The team is composed of one DR with HDR (the team leader) and three equivalent CR. It is attractive and was reinforced in 2021 with one CR.

During the 2016–2021 period, the team identified new mechanisms for the regulation of Mus81-Eme1 that rely on phosphorylation of Eme1 by cell-cycle control and DNA damage signalling kinases and on SUMO-binding properties of Eme1. It also demonstrated that SLX4 and RTEL1 are direct binding partners and that SLX4-RTEL1 complex formation is required to prevent transcription-mediated perturbations of DNA replication. The team also characterised a role of SLX4 in the modulation of mismatch repair and SLX4IP-dependent contributions in telomere maintenance. This work led to original publications in high impact journals (1 Mol Cell 2019 in collaboration, one NSMB 2020 as first and last author) and more recent work was uploaded in BioRxiv in 2021 and lead to two publications as PI in 2022 (1 PLOS Genet 2022, 1 NAR 2022). The team also signed as main author three excellent reviews that are references in the field (1 Nat Rev Mol Biol Cell, 1 Crit Rev Biochem Mol Biol, 1 Curr Opin Genetics Dev).

The team was successful in grant funding during the complete period with 2 INCa PLBIO as coordinator in 2017 and in 2019. The team received the prestigious label 'Équipe FRM' from the foundation as a single team in 2021. Members participated to the assessment of grant applications as external reviewers and/or members of scientific communities (Ligue contre le Cancer, Fondation ARC, PACA Canceropole). The team leader was also invited to international meetings of high visibility in genome integrity (for example, two EMBO workshops in 2017 and 2019 and the IBS conference in South Korea in 2022).
The team hosted four postdoctoral fellows, funded by INCa (3) and ARC (1). One is still ongoing.
The team is well integrated in the CRCM with ongoing collaborations with the teams of Mauro Modesti, François Bertucci and Emilie Mamessier, Vincent Géli and Stéphane Coulon and more recently initiated projects with potential economic impact with the Morelli-Colette team to find inhibitors of the SLX4-SLX1, SLX4-MSH2 and EXO1-MSH2 interactions. The team also built translational projects with collaborators from Gustave Roussy on metastatic breast cancer.

Weaknesses and risks linked to the context

The team trained only one PhD student during the 2016–2021 period and mentions difficulties to recruit well-trained students motivated for basic science.

RECOMMENDATIONS TO THE TEAM

The team is encouraged to increase its international visibility through participation in conferences and to apply for ERC grants.
The team feels limited by its publication rate and its attractiveness (departure of postdocs, difficulty to recruit PhD students). The committee encourages being proactive in finding a solution to attract good PhD students (for example be involved in Master formation and apply to A MIDEX calls with international collaborators).

Team 10: Telomeres and chromatin

Name of the supervisor: Mr. Vincent GÉLI

THEMES OF THE TEAM

Using budding and fission yeast, the team investigates the replication and the maintenance of telomeres in the context of telomere erosion. The team also studies the dynamic and maintenance of telomeres in replicative senescence or during quiescence. The team has additional interest for histone metabolism and the Set1 complex that methylates the Lysine 4 residue of Histone 3. The team has also been involved in several cancer projects in collaboration with other groups of the CRCM.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Overall, the last evaluation of the team was excellent and the HCERES experts underlined its outstanding reputation and know-how. One weakness was, however, identified and the recommendation was to explore options for partnerships with industry. Along this line, the team has established, in coordination with the team of C. Lachaud, a partnership with Genomic vision for the exclusive implementation and development of a technology to measure telomere length. The team also mentions that technological resources with economic value are developed in the context of the REPETOMIC e-Rare international consortium coordinated by V. Géli. The team also shared its knowledge with the general public through general public conferences over the past five years.

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	3
Scientist (Chargé de recherche, CR) and associate	6
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	2
Subtotal permanent personnel in active employment	**11**
Non-permanent teacher researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	0
Post-docs	3
PhD Students	4
Subtotal non-permanent personnel	**7**
Total	**18**

EVALUATION

Overall assessment of the team

The research performed by the team is outstanding with an impressive scientific production in the field of telomeres and chromatin replication. The team is internationally recognised and highly productive. Many research projects are currently running that, in some instances, involve collaborations with recognised experts in the field. The attractiveness of the team is excellent to outstanding, as assessed by the recruitment of permanent and non-permanent staff and by obtaining regular funding. The team has organised scientific conferences and is highly visible. The overall assessment of the team is outstanding.

Strengths and possibilities linked to the context

The team is working on various aspects of telomere biology using either yeast as model system or human cells. They also have a strong interest in histone metabolism with a specific focus on the Set1 complex. More recently, they started working on a preclinical knock-in model in which *Tert* gene expression is driven by the senescence-induced *p21* promoter. This system thus allows addressing whether telomerase expression in pre-senescent cells may avoid the appearance of some of the age-associated dysfunctions including emphysema, pulmonary perivascular fibrosis or metabolic dysfunction.

The scientific production of the team is outstanding over the last five years, publishing as PIs, in very high impact journals including two Cell Reports (2016, 2020), two Nat Commun (2017 and 2020), Sci Adv 2018, Nucl Acids Res 2020, Mol Cell 2019, Elife 2018, and several papers deposited in BioArXiv and published in 2022 (EMBO J 2022, EMBO Mol Med 2022). Importantly, all the tenured researchers have contributed to the scientific production of the team and PhD students have published either as first or co-first author. Similarly, postdocs have been published as either first or co-first author in prestigious journals (EMBO J, Cell Reports…).
The team has an excellent to outstanding international visibility; the team is involved in fruitful collaborations with high-level partners from all over the world in the field (Buratowski, Harvard…). The team has secured a number of funding in local or national calls: with the team leader as PI and coordinator: INCa-PLBIO (2019-2022), ANR-Thalatel (2023-2025), ITMO equipment, e-Rare consortium, ANR Cistransloop. Labellisation Ligue (2021–2023), Inserm AGEMED (2021–2023), Interaging program (2023–2025); with members as PI and coordinator (ANR TeloRP) and partner (ANR TeloMito, ANR Niro).
The team has established, in coordination with the team of C. Lachaud, a partnership with Genomic Vision for the exclusive implementation and development of a technology to measure telomere length. The team has also initiated fruitful collaborations with P. Revy (Institut Imagine, Paris) and C. Kannengiesser (Hôpital Bichat, Paris) on telomeropathies, which is clearly an added value with exciting and promising translational perspectives.
The team is also very active in organising scientific meetings or conferences and benefits from international recognition in the field. PIs from the team are regularly invited to give talks in international scientific meetings (International Conf on aging, China; International nuclear transport meeting…).

Weaknesses and Risks linked to the context

The work with the knock-in (KI) model detailed above has been running for a while but did not yet get to publications. It seems, however, that two manuscripts are either submitted or in preparation that will hopefully lead to publications.
There seems to be many different research projects (telomeres, histone biology, senescence, metabolism, G4C2 triplet expansion, TOP3A…) and model systems (*S. cerevisiae*, *S. pombe*, *human cells*) for a same team.
There may be some problems getting grants for a project.
Despite its international recognition, the ERC advanced grant application by the team leader to explore the potential antagonistic roles of p21Cdkn1a and TERT in hypothalamic senescence and self-renewal as drivers of metabolic dysfunction was not selected after step 2, a main concern being the lack of experience in brain biology.

RECOMMENDATIONS TO THE TEAM

The team may find useful to think about the gain/risk ratio of a project and the physiological questions that can be addressed by this model, including with the catalytically dead telomerase mutant. Recruiting permanent researchers on this highly competitive topic may also be useful. The team may also increase collaborations with the IPC to analyse tumour samples. The work on TOP3A and ALT for instance may clearly benefit from such interactions.
The PI is encouraged to renew his application for an ERC Advanced grant.

Team 11: Pancreatic cancer

Name of the supervisor: Mr. Juan IOVANNA

THEMES OF THE TEAM

The scientific activity of the team 11 is focused on pancreatic adenocarcinoma. This area of research is seen as a priority in Cancer Research given the urgent need to improve the knowledge and care of this very deadly cancer currently without effective treatment and whose incidence is increasing dramatically in western countries. The objectives of Team 11 research are to increase knowledge on this disease and try to use novel targets and/or biomarkers to improve treatments, diagnosis and prognosis of patients. They focus on:

(i) the role of stress genes in tumour progression and their use as potential new therapeutic targets
(ii) the rewiring of metabolic, energetic and signalling (inter, intracellular) pathways occurring in tumour cells
(iii) the dialogue between tumour cells and their microenvironments
(iv) the molecular mechanisms of resistance to therapeutic treatments, and
(v) the multi-omic analyses and signatures-based stratification of pancreatic tumours.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The main recommendation was to keep going on their excellent fundamental and translational research with encouragement to try to transfer to the clinic and publish in prestigious journals, to apply for ERC grants and to convert some patents into licences. Not all of the aspects of this, overambitious call to become even more excellent has been achieved, but some were. Hence the team has repeatedly published in the best high-audience journals (EMBO J, PNAS, EMBO Mol Med, JCI, Nat Commun, Cell Rep, Cancer Res, Clin Cancer Res, Ann Oncol, etc.)., has converted several patents in licences and creation of biotech start-ups, and clinicians associated with the team have been involved in several clinical trials with some based on research developed in the team.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	6
Lecturer and associate lecturer	4
Senior scientist (Directeur de recherche, DR) and associate	6
Scientist (Chargé de recherche, CR) and associate	5
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	10
Subtotal permanent personnel in active employment	**31**
Non-permanent teacher researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	2
Post-docs	5
PhD Students	6
Subtotal non-permanent personnel	**13**
Total	**44**

EVALUATION

Overall assessment of the team

The last two decades this very large team has built a unique pancreatic cancer program, and since its merger with the CRCM, is a true asset for the institute. It stands by its outstanding records in terms of scientific activity, attractiveness and activities connected to the socio-economic world.
The current team staff must be congratulated for having been able to initiate, develop and maintain the cohesion of such exceptional team over a long period of time, establishing a multidisciplinary team with a leadership position in France and an unquestioned international reputation on pancreatic cancer. This large group will be split into two teams for the next term (2024–2028). The HCERES panel strongly recommends that the two future teams remain tightly connected with joint objectives and sharing. The overall assessment is outstanding.

Strengths and possibilities linked to the context

The team had developed in house/in team complementary expertise. It is composed of scientists & clinicians with complementary clinical activities, a true and unique asset in the field of pancreatic cancer.
Organised in several subgroups each with its own Principal Investigator (Scientists), funding and specific, although complementary, objectives.
The team has made important contributions in different areas of pancreatic cancer. A large variety of molecular, cellular and ex vivo or in vivo/preclinical tools and models have been generated and a wide range of topics have been explored over the evaluated term. The tight connection with clinicians allowed privileged access to unique collections of high quality patient samples and clinical data. Hence one of the major contributions has been to better characterise pancreatic adenocarcinomas at the multi-omics level and to create very valuable and large collections of well characterised patients-derived xenografts (150 PDX), patient-derived organoids and primary cell lines. This makes the team a leader in France in this respect.
These valuable collections and multiple omics analyses allowed the description of different subtypes of tumours and of clinically relevant signatures predicting the response to different treatments that were patented and transferred to biotech.
Using these valuable collections and signatures, all the subgroups have also significantly contributed to the basic knowledge of pancreatic cancers biology and to the identification of new biomarkers and potential targets to improve treatments, prognosis or stratification of patients. These scientific discoveries concerned stress proteins, metabolic rewiring, mitochondrial activities, tumour microenvironment, or post-translational modifications of pancreatic tumours. Many of these studies have led to preclinical validations and some to the development of new inhibitors with anti-tumour properties.
This work led to an excellent scientific production with more than 150 scientific publications, *a* large part of them in PDC. These articles have been published in journals of various levels including in the most prestigious one (*EMBO J, PNAS, EMBO Mol Med, JCI, Nat Commun, Cell Rep, Cancer Res, EBiomedecine, Clin Cancer Res, Ann Oncol, etc*.)., and some were widely publicised and highly cited. This work also led to numerous invitations and participation to national and international meetings. Altogether, this record confirmed that the team as a whole has achieved excellent national and international visibility on pancreatic cancers.
The Team has developed numerous international collaborations including with the most prestigious laboratories in their field that led to collaborative publications in prestigious journals, highlighting again its leadership at the international level.
The team as a whole has been very successful in obtaining large or small national grants (>35) from French governmental agencies (several PAIR Pancreas, PRTK and PLBIO from INCa, Canceropole, SATT, BIP, Inserm-transfer, etc.) or from charities (continuous labelisation LNCC, labellisation ARC, CIT LNCC, FDF, ARC, BMS, etc...)
Some of the team's work (inhibitors, omics signatures) also led to a remarkable activity of valorisation through the filing of eight patents, including two with licenses, and to the establishment of collaborative contracts with companies or start-ups interested in pancreatic cancer. Noticeably, based on team discoveries and reagents, several members of the team have been directly involved in the creation of two of these biotech companies (PanCa Therapeutics, PredictingMed) and several others play active roles in these companies.
The team has hosted fifteen PhD students, most of them having published their results in international journals and produced review papers.
Members of the team regularly participate in scientific committees and councils for government agencies or charities, at local, regional, national or European levels.

Weaknesses and risks linked to the context

Although the scientific activity of the team focuses exclusively on the study of pancreatic cancer, the numerous distinct projects, each with its own principal Investigator, result in dispersion that dilutes the visibility of expertise.
The links and intra-team collaborations between the various sub-groups could be strengthened.

This large and successful team is currently organised in several subgroups each with its own Principal Investigator (Scientists), funding and specific objectives. The team will be split into two teams for the next term (2023–2027), a split planned since 2020 and approved by the international SAB of the CRCM. The review panel questions the consequences of this planned split of the current team on its leadership, national/international visibility and attractiveness. The strategy to maintain this link at all levels could be better described.
Solid tumour research is evolving rapidly with the advent of a single cell and spatial studies, a move that the team has not, yet achieved.
The strategy and positioning of the team and of the CRCM, and its evolution, in regard to the biotechs created by the members of the team, is not yet well defined.
The team's communication to the general public and media is underdeveloped considering the team's impact in the field of pancreatic cancer in France.
Despite the excellent positioning and international visibility of the team in its field, the application and success in obtaining international funds have been limited.

RECOMMENDATIONS TO THE TEAM

This large group will be split into two teams for the next term (2023–2027), a split planned since 2020 and approved by the international SAB of the CRCM. The HCERES panel strongly recommend that the two future teams remain tightly connected with joint objectives and the sharing of expertise, models and results that have made it so successful.
The two future teams need to better define the strategy and positioning of the team (and of the CRCM), and its evolution, in regard to the biotechs created by the members of the team.
Even if there is a good and recognised expertise of the team in the field of pancreatic carcinoma, it could be recommended to refocus on a more limited number of themes.
It will be interesting to compare the team's results obtained on pancreatic with other digestive cancers such as biliary truct cancers and more particularly cholangiocarcinoma
Solid tumour research is evolving rapidly with the advent of a single cell and spatial studies, the team (or future teams) should position itself on these approaches. The team's communication to the general public and media should be improved, especially since the team's impact in the field of pancreatic cancer in France is such that it is worthwhile.
Considering the excellent positioning of the team in its field, the review panel strongly encourages the team to pursue its efforts to obtain international funding and recognition (in particular at the European level, i.e. ERC, Mission Cancer, HSFP Transcan, EuroPDX, etc.).

Team 12: Genome Dynamics and Recombination

Name of the supervisor: Mr. Bertrand LLORENTE

THEMES OF THE TEAM

The team is working on the process of homologous recombination, specifically on meiotic recombination in budding yeast. Both theoretical and methodological approaches are used to explore this process.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

From 2016 to 2021, the team has satisfactorily responded to recommendations made in the previous report. The group has published twelve papers in internationally recognised journals with more or less broad readership. Several of these papers have made an important impact on understanding meiosis and genome evolution. Notably five papers published as last or co-corresponding author in Genome Research (2016), two PLOS Genetics (2017, 2022), Molecular Cell (2018), Yeast (2021) testified to the quality of the work done by the team. Other papers produced in collaboration with internationally recognised French and international colleagues demonstrated the high value of the work performed.

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	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)	0
Subtotal permanent personnel in active employment	1
Non-permanent teacher researchers, researchers and associates	**2**
Non-permanent research supporting personnel (PAR)	0
Post-docs	1
PhD Students	0
Subtotal non-permanent personnel	2
Total	**3**

EVALUATION

Overall assessment of the team

The scientific production of the group is outstanding with five papers in primary journals including Nature (co-author) and Molecular Cell (PI) where group members were either leader or co-leader of the study and with five papers in collaboration. The visibility of the team is excellent in the field of meiotic recombination, of genome stability and evolution in yeast species by its seminal studies. It is part of an excellent national network of yeast geneticists and was regularly successful in grant funding as PI. The global assessment of the team is excellent to outstanding.

Strengths and possibilities linked to the context

The research performed by the team is outstanding: the team has been very productive over the current period of review by producing ten papers in total, including five papers as leading/corresponding author in primary journals (Genome Research – 2016 –, 2PLOS Genetics – 2017, 2022 –, Molecular Cell – 2018 –, Yeast – 2021 – and six papers as co-author – Nature, two in PLOS Genetics, G3, Nucleic Acids Research, Mol Syst Biol, ELife, FEMS Yeast Res –. The audience of several of these papers is high – Molecular Cell, Nature, MolSys Biol –. According to the small size of the group, all the publications from the team involve co-authorships with internationally recognised colleagues.

The team has an excellent visibility because of their seminal studies with an original assay to characterise meiotic heteroduplex DNA tracts genome wide. They are well integrated in excellent national networks of geneticists and biologists interested in meiosis, genome stability and evolution in yeast that organise regular meetings and favour collaborations between teams.

The projects are regularly funded by national agencies as principal investigator – PI – in three ANR, one ARC project and Emergence Canceropole PACA; and partners in one ANR.

Members have been invited to international meetings as FASEB, the USA, and emerging concepts in chromosome biology in Austria.

Three PhD defences were supported and two postdocs hosted.

Weaknesses and risks linked to the context

The main weaknesses of the team are its small size and the difficulty to attract good PhD students. Also, one permanent researcher left the team in 2019.

RECOMMENDATIONS TO THE TEAM

The team should continue to perform important and fundamental work on genome stability and evolution in the well-adapted yeast model. The team should recruit permanent staff to reinforce its visibility and long-term development.

The team is also encouraged to consider how far these mechanisms are conserved in human cells and their impact in human cancers through collaboration with the team within its department and the CRCM.

Team 13: Homologous Recombination, NHEJ and Maintenance of Genomic Integrity

Name of the supervisor: Mr. Mauro MODESTI

THEMES OF THE TEAM

The team is working on the process of double-strand break repair mechanisms in human cells. They use a variety of biochemical approaches to analyse the relevant DNA/protein transactions at the molecular level.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous evaluation recommended a focus on leading three promising and exciting projects and indicated that attention should be paid to try to increase international visibility. The group is nowadays internationally recognised on three main topics: study of the human NHEJ mechanism, study of human RAD51 and its control, study of human RAD52; study of the DNA interaction of human MRE11/RAD50/NBS1.

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	1
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	0
Non-permanent research supporting personnel – PAR –	1
Post-docs	1
PhD Students	1
Subtotal non-permanent personnel	**3**
Total	**4**

EVALUATION

Overall assessment of the team

The scientific production of the team is outstanding with six publications in highly ranked journals where group members were either leader or co-leader in the study and 21 collaborative publications, many in high impact journals. The group has an excellent to outstanding international visibility in the field of genetic recombination and the maintenance of genome integrity. The group is involved as main PI or as partner in thirteen national and international collaborations with leaders in the field through his exceptional expertise in biophysical, biochemical or imaging approaches. Overall, the research performed by the team is outstanding.

Strengths and possibilities linked to the context

This is a relatively small team composed of three CNRS staff scientists – one DR, one CR and one IR; the CR and the IR left the group in 2019 – , five PhD students and five postdocs over the period. Three PhD theses have been defended over the period.
The scientific production of the team is outstanding with a total of 27 publications in prestigious journals, as PI or collaborator. The PI is corresponding author of six papers published in Cell Reports – 2016, 2017 –, ELife – 2017 –, PLOS Genet – 2019 –, of one Opinion paper – Science 2018 – and of one review – Curr Opin Genet Dev, 2021 –. For eleven of the collaborative papers – Nature, Methods Mol. Biol. Nature Structural and Molecular Biology … – , the PI is the only author of the group.
The team collaborates with thirteen recognised groups over the world – six in the US, two in Netherlands, two in France, three in other countries – through its exceptional expertise in biophysical, biochemical and cell biology approaches. The group has an excellent to outstanding international visibility.
Regarding funding, the team was successful in getting various national grants: one ANR, one INCa PLBIO, one ARC and one Label Ligue as coordinator and three ANR and two INCa as partner.
The team leader submitted an ERC in 2017 and 2019 but did not pass the first selection step. He therefore submitted the project to the French League against Cancer and got funded for five years. This year, he submitted an HSFP letter of intent that was not selected. The team was accepted in the CENTURI Network of the AMU which aims at promoting interdisciplinarity.
The PI has gained an international reputation as attested by the invitation to write perspectives and reviews in high audience journal as Science and Current Opinion in Genetics and Development. He was an invited speaker in FASEB, 3rd DNA replication/repair structures and cancer conference,
The team hosted three PhD students and three postdocs during the mandate.
The team has a number of interactions with other teams of the CRCM that led to one publication in Oncoimmunology and one manuscript is in preparation.
The non-academic activity of the team is very good with the submission of a patent.

Weaknesses and risks linked to the context

Because of the many collaborations, members of the group, especially PhD students – two out of three who graduated –, are not first author of the publications; this might be prejudicial for their career and the possibility to get a competitive permanent position.
The team has a small size and the PI is nowadays the only permanent staff.

RECOMMENDATIONS TO THE TEAM

There is a need to reinforce the leadership of the team on a limited number of topics to ensure that group members are first or co-first authors and to attract permanent scientists in the team. The team is also encouraged to reinforce collaborations with teams from the CRCM and with the IPC to characterise the involvement of processes under study in human cancers.

Team 14: Immunity and Cancer

Name of the supervisor: Mr. Jacques NUNÈS and Mr. Daniel OLIVE

THEMES OF THE TEAM

The main research focus of the 'Immunity and Cancer' team is the study of the cells and receptors involved in tumour immune response. The team is also involved in the development of novel strategies of immunotherapy in cancer patients. The team is particularly interested in:

i) The functions of molecules belonging to the CD28/B7 and TNF/TNFR families involved in the regulation of the immune system and that is a major target for new therapeutic strategies,

ii) The activation of the phosphatidyl-inositol 3′ -kinase (PI-3K) signalling pathways after T Cell Receptor activation and/or costimulatory molecules binding in both T and NK cells.

Also, the team is involved in the immunomodulation following allogenic stem cell transplantation (aSCT) through its participation in several clinical trials.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

One of the recommendations was that the team should make an effort to limit the extent of the proposed research. Although the numbers of projects did not decrease, a former postdoc of the team got a permanent position at INSERM reinforcing the number of researcher PI in the team. It had also been recommended to anticipate the succession of MD professor (one of the team's PIs) by recruiting a young professor of immunology to take the lead of the important translational work managed by the senior PI. Several PU-PH develop translational research in the team and could take the succession of senior team leader.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	6
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	0
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1.5
Subtotal permanent personnel in active employment	**9,5**
Non-permanent teacher researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	1
Post-docs	3
PhD Students	6
Subtotal non-permanent personnel	**10**
Total	**19.5**

EVALUATION

Overall assessment of the team

The research performed by the team is outstanding with a remarkable scientific production from basic to translational and clinic research in the field of immuno-oncology. The team is very well recognised at the international level, and was successful in grant funding and particularly in contracts with international pharma industries, its attractiveness is outstanding. Due to the involvement of one PI in the development of several biotechs based on his research works, the team has an outstanding level in valorisation. The global assessment of the team is outstanding.

Strengths and possibilities linked to the context

This is a large research team (composed by an impressive number of scientists, professors, clinicians, technicians, postdocs and PhD students) that established a solid network of collaboration with both the clinic and the industry.
The PIs are competent and well recognised in the field of tumour immunology at both national and international level. The team provided important contributions to the field of immunology.
The output is remarkable in terms of the number of publications: 459 publications (2/3 of these publications are from clinical studies associated with team members and about 50% of original articles are signed by at least one member of the team in good position. The articles, as PI, are published in PNAS, Blood Adv, Front Immunol, Cell Reports…).
The team has built a real continuum from basic to translational research in the field of immuno-oncology and the PIs are inventors of 24 patents during the period 2016–2021, eight have been licensed.
Basic research of the team is now translated into clinical trials via notably the development of therapeutic antibodies and the generation of four spin-offs: ImCheck Therapeutics, Alderaan Biotechnology, Emergence Therapeutics, Stealth IO. These collaborations give new insights in the basic research of the team.
The team is deeply involved in education through the presence of several PU-PHs and MCU. Fourteen PhD defences were supported, twelve are ongoing, nine postdocs hosted with three postdocs still present. All have at least one paper in first position.
Team members and PIs are involved in three platforms (cytometry, immunomonitoring and facility) and developed innovative technological approaches in the field of cytometry (several members of the team are participating to national cytometry networks and are running some national education programs in cytometry – formation permanente Inserm – .
The team have secured a large amount of funds from regional – Canceropole – and national grants – ANR, INCa – , from charities as ARC, and the prestigious label 'Équipe FRM' but also many contracts with biotechs – GSK, Sanofi, Cellectis, BMS, etc. —.
PIs are often invited to present their work in national and international conferences or meetings – Protein Engineering & Cell Therapy Summit – PEGS – Boston –; Virtual lymphocyte signalling symposium – Siena –; International Cytometry symposium St Etienne –; Transplantation Society Meeting, Shanghai) or to give a lecture in international Institutes or universities (keynote lecture at the Académie royale de médecine de Belgique, lecture at the Humanitas Research Hospital – Milano).

Weaknesses and risks linked to the context

Many axes from basics, to translational and clinic research are developed in the team.

RECOMMENDATIONS TO THE TEAM

A better integration of all the studies performed across the team will be necessary and will be the next challenge considering the very large team.
Although each axis is supervised by a permanent researcher or clinician, the PIs of the team must be careful to avoid the dispersion of projects.
A professor-PH will have to take the lead of translational works to allow the team to carry out the projects from basic to translational research in the field of immuno-oncology when the senior team leader PI retires.

Team 15: DNA damage and genome instability

Name of the supervisor: Mr. Vincent PAGÈS

THEMES OF THE TEAM

The main goal of the team is to understand the biological consequences resulting from the replication of a damaged genome that is at the origin of cancers. For this purpose, the team has developed a unique technology allowing the insertion of a single lesion at a specific site of the bacterial chromosome (recently this method was extended to yeast). This approach enables to follow *in vivo*, the distribution between translational synthesis and damage avoidance in different genetic backgrounds.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

One of the main recommendations of the previous evaluation was to increase the visibility of the PI by acquiring complete independence. Within this framework, thanks to four articles in Nucleic Acids Research as a sole corresponding author and two reviews as an invited author, the PI clearly demonstrated his independence.
During the previous evaluation, the committee of experts recommended exploring possibilities for knowledge transfer of the unique technology. This recommendation was not considered as opportune by the PI since the technology that helps answer fundamental questions seems not to be of interest for the industry.
The PI was also encouraged to interact more with groups outside his own area of research. Thus, in addition to already established collaborations with the teams 9 and 13 of CRCM, new collaborations with teams 17 and 20 have been initiated.

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	1
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)	1
Subtotal permanent personnel in active employment	**3**
Non-permanent teacher researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	0
Post-docs	2
PhD Students	1
Subtotal non-permanent personnel	**3**
Total	**6**

EVALUATION

Overall assessment of the team

The team develops excellent scientific research projects that led to the publication of articles in the best journals of their disciplines. Its attractiveness is very good to excellent with the obtention of several grants in response to competitive calls as principal investigator (ANR JCJC, Equipe FRM, ARC). The team also has a very good record of outreach activities. The overall assessment of the team is excellent.

Strengths and possibilities linked to the context

The team is composed of one DR (HDR, team leader) one postdoc from the team recently obtained a tenure position, and a permanent staff, a CNRS IE and two postdocs. While the team has supervised only one PhD student (2017), two postdocs and numerous trainees (12) were hosted during the evaluation period.
The team developed a unique scientific approach in order to introduce a single lesion in the genome of a living cell. The uniqueness of this technology offers to the team a high visibility at the national and international levels.
The team has published six scientific articles including four original articles, one review and one book chapter. The PI was the corresponding author of nearly 90% of the whole scientific production. Four articles were published in a high impact journal as PI (Nucleic Acids Research) attesting of the high quality of the research developed by the team.
Between 2016 and 2021, the team initiated new internal collaborations with two other teams of the CRCM (teams 17 and 20) as well as international collaborations with research groups from Osaka University (Japan) and Harvard Medical School in Boston (USA), attesting of the interest aroused by their technology. The team leader was a speaker at several meetings (IMB/SFB 1361 conference; Germany, 5th German-French DNA repair meeting; 4th, 5th and 6th DNA Polymerases Meetings, France, Netherlands and Sweden…).
The team is a laureate of the prestigious '*Équipe FRM*', one ARC grant and one ANR young investigator (2017–2019).
The PI has taken part in several outreach activities (participation to '*LesChercheursMobilisés*' organised by the FRM, one article in Médecine/Sciences, interview to the local press).

Weaknesses and risks linked to the context

The scientific policy of the team lacks of transfer strategy towards the socio-economic world.
The attractiveness of the team seems to be relatively weak for recruiting PhD students.

RECOMMENDATIONS TO THE TEAM

The team should pursue its effort to increase its manpower by recruiting senior postdoc researchers eligible to obtain a permanent position at CNRS or INSERM.
The team should continue to develop new collaborations (local, national and international) in order to further demonstrate the usefulness of its unique technology in the field of cancer.
A real policy of transfer towards the socio-economic world should be envisaged not only to valorise the research by potential applications but also to obtain financial support from the industry.

Team 16: Spatio-Temporal Regulation of Cell Signalling – Scaffolds & Phosphoinositides

Name of the supervisor: Mrs. Pascale ZIMMERMANN

THEMES OF THE TEAM

The team focuses on the molecular mechanisms supporting exosome biogenesis, loading and uptake, scaffolding proteins (heparan sulfate proteoglycans and PDZ domain proteins) and phosphoinositides, which play an important role in the spatiotemporal organisation of intracellular signalling. The team oriented work towards biotherapies and pharmaceutical innovation, developing synthetic biology strategies for the vectorisation, loading and high-yield production of therapeutic nano-sized extracellular vesicles. The team also developed and validated small pharmacological inhibitors of PDZ interactions.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The main recommendations of the previous evaluation was to increase the manpower of the team in terms of PhDs/postdocs and PIs. One MCU has been hired during the period. In regard to the few numbers of people, the low level of outreach activities is unchanged.
Translational research has been started since the team oriented work towards biotherapies and pharmaceutical innovation (inhibitors of PDZ interactions, therapeutic nano-sized extracellular vesicles…)

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	1
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	0
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	**4**
Non-permanent teacher researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	0
Post-docs	1
PhD Students	1
Subtotal non-permanent personnel	**2**
Total	**6**

EVALUATION

Overall assessment of the team

The team exhibits both an excellent level of publications in high-level journals of the field (Nat Comm, PNAS, J.E.V…) and attractiveness with a shared laboratory in Belgium. The capacity of the team in terms of valorisation is very good with innovative pharmacological developments. The scientific topics related to cancer are dedicated to a very fundamental research axis, which helps the international recognition of the site. Translational projects are developed and allow the integration of the team in the centre. The PI shows an international reputation and partnerships.

Strengths and possibilities linked to the context

The team exhibits a high level of publication (153) most of them involving the team leader (140) and some of them with a double geographical attachment: CRCM and Department of Human Genetics, Katholieke Universiteit Leuven, Belgium. The team authored, as PI: Nat Commun 2016, PNAS (2016, 2020), Scientific Rep 2021, Front Cell Dev Biol. 2022 (review). The publication in PNAS in 2020 of a study carried out in collaboration with J.P. Borg's team has improved the team's visibility within the CRCM.
The scientific topics related to cancer are dedicated to a very fundamental research axis, which helps the international recognition of the site. Translational projects are developed (validation of small pharmacological inhibitors of interactions with PDZ domains and synthetic biology strategies for the delivery, loading and production of therapeutic extracellular vesicles of nanometric size).
The team shows an international reputation and partnerships as demonstrated by invitations to meetings (Keynote in the meeting of the German Society for EVs 2018; main organiser of the second annual meeting of BESEV as a joint meeting with the Belgian Society for Cell and Developmental Biology – BSCDB – 2019; invitation to Keystone symposia 2020.).
The team had its own funding and obtained financial support from the site (notably AMIDEX funds), from LNCC Label and ANR (2019–2023). Other funding was obtained from charities as *Fondation de France and ARC*.
AMIDEX funding indicates a willingness of the CRCM to integrate the team.
Two PhD defences were supported and five postdocs were hosted. All were publishing.
The team includes two engineering assistants and a recently hired MCU of Aix-Marseille University.

Weaknesses and risks linked to the context

Although a MCU recently joined the team, it is of very small size and no indication appears related to the recruitment of researchers. At the level of the team, training through research is very low in terms of students and postdoctoral fellows (3 PI and 1 postdoc).

RECOMMENDATIONS TO THE TEAM

The strengthening of manpower must be pursued in order to stabilise and develop the main projects.

Team 17: Predictive Oncology

Name of the supervisor: Mr. François BERTUCCI and Mrs. Émilie MAMESSIER

THEMES OF THE TEAM

The team focuses on the study of advanced, therapy-resistant forms of breast and colon cancers. The investigators follow a primarily translational approach with observations in the clinic, followed by the study of mechanistic aspects by various methods. The team is specifically interested in cancers that are aggressive and resistant to systemic treatments. They develop three axes of research:

(i) they profile clinical samples (primary and metastatic tumours) for a better characterisation of genomic landscapes and better prognostic/predictive classification, and identification of clinically relevant targets

(ii) they use markers and models to understand the mechanisms of resistance to treatment and

(iii) they design new treatments to target/overcome resistance to treatment.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Among the recommendations of the previous report, the SAB felt that the group has nicely exploited its great resources and has reached a high international visibility, in particular in the translational area.
The SAB encourages the group to more precisely define a 5-year perspective, and to strengthen their links to basic science groups within the CRCM. The team has partially taken under consideration the recommendations of the previous report (concerning the 5-year perspectives) notably by developing ideas, projects and novelties related to new treatments approved or under development in clinics.
The HCERES recommendations were to publish in journals with higher audience and increase international visibility. The team developed many collaborations with groups within the CRCM (but not particularly with basic science groups) and among the publications issued from collaboration with these other teams, 55% of them are published in recognised and prestigious international journal such as *Eur J Cancer (*2021), *Nature (*2019), *Cancers (*2019). The team also increased its international visibility (invitations, etc.).

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	4
Lecturer and associate lecturer	4
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)	9
Subtotal permanent personnel in active employment	**21**
Non-permanent teacher researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	2
Post-docs	1
PhD Students	6
Subtotal non-permanent personnel	**9**
Total	**30**

EVALUATION

Overall assessment of the team

The team has an outstanding scientific activity with 75 articles as PI in Nature, Lancet Oncol, etc. Attractiveness is outstanding regarding funding and international invitations and visibility. Public outreach can be improved. The overall assessment is outstanding.

Strengths and possibilities linked to the context

The team regroups people with multiple competences: scientists (engineers, molecular and cellular biologists, biocomputational analysts, chemists…) and clinicians (medical oncologists, surgeons, haematologists) working in tight collaboration on translational research programs. The team has multidisciplinary competences insured by bioinformaticians, molecular & cell biologists, biochemists, clinicians. One of the strengths of the team is the complementarity of the two co-leaders (clinician and scientist). The team develops many ideas, projects, novelties notably related to new treatments approved or under development in clinics.
The team has a high visibility in the scientific community. Members have contributed to more than 200 publications indexed in PubMed, over the 2016–2021 period. More than 75 of these publications are original reports issued from the team. The team has an excellent level of publications in international peer reviewed journals with strong visibility, both for the scientific and the clinical communities (2 Lancet Oncol in 2016; 2 Annals of oncology,2017, 2018; Genome Med. 2021, Eur J Cancer 2021, Nature 2019 cited 275 times, Cancers 2019, J. Clin Med. 2019…). Funding was obtained from ANR, Ligue contre le cancer (Labelisation), Canceropole, INCa PLBIO, Fondation de France and some industrials (Lilly, Pfizer, EDF foundation, Ruban Rose, …). The team expertise is recognised at a national and international level as revealed by numerous invitations to meetings (International Inflammatory Breast Cancer Conference, Morgan Welch Inflammatory Breast Cancer Research Program: 10th Anniversary Conference…) and seminars (International seminar, Harvard; Emerging technologies in therapeutic oligonucleotides, Cambridge – UK – …).
The team has access to a large biobank of clinically well-annotated primary patient samples derived from clinical trials (e.g. PERMED-01, -02; Neo-R trial), in part also involving new signalling inhibitors (CDK4/6 and PIK3CA inhibitors).
Members have started to successfully set up the platform of patient-derived organoids that will allow the investigators to evaluate tumour sensitivity, and to study resistance mechanisms to various approved or novel compounds.
PhD students (12 hosted) and postdocs (3) are mainly involved in the experimental part of the scientific projects carried out in the team. They are also involved in the data analysis and the communication of the results.
The team received two prices at the *Association pour la Recherche sur le Cancer 2018*.
Three patents have been filled.

Weaknesses and risks linked to the context

We can point to the fact that there is a poor participation to the scientific committee and evaluation committee.
The recruitment of postdoc is limited and even if there is student attractiveness, it is noticed a small pool outside MDs

RECOMMENDATIONS TO THE TEAM

It could be recommended to the team to focus more on a few cancer types in order to gain in visibility in their field of interest. This should help them improve their publication. Public outreach should be increased.

Team 18: Epithelial stem cells and cancer

Name of the supervisor: Mrs. Emmanuelle CHARAFE-JAUFFRET and Mr. Christophe GINESTIER

THEMES OF THE TEAM

This team combines fundamental and translational aspects of research on cancer stem cells. They decipher molecular mechanisms driving the susceptibility of a cell-of-origin to be transformed by a specific oncogenic event. They also explore cancer stem cell fate and develop new strategies to target these cells to overcome tumour recurrence. They have established and benefit from a very valuable collection of well-characterised breast cancer pdx and associated databases and biobank. More recently, to address the question of the cell of origin in both the mammary gland and anorectal tissue junction, they also developed original ex vivo 3D models (organoids/tumoroids), as well as cellular and preclinical models for tracking and screening approaches.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The main recommendation of the previous evaluation was to improve international collaboration network of the team's, especially with a lead position. Recommendations were expressed to attract, permanent researchers, postdocs and PhD to remain competitive. At the scientific level, the team not only maintained but strongly increased its outstanding production as attested by major publications in PDC. Regarding the manpower, the team remained a little undersized with three CRCN, one DR and one PU-PH as permanent full-time researchers. A postdoc has just been recruited. Nevertheless this does not affect the production and collaboration capacity of the team. An international collaboration with a team in the USA has been set up.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	1
Lecturer and associate lecturer	1
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)	2
Subtotal permanent personnel in active employment	**7**
Non-permanent teacher researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	2
Post-docs	0
PhD Students	4
Subtotal non-permanent personnel	**6**
Total	**13**

EVALUATION

Overall assessment of the team

The research of this group is outstanding with major breakthrough contributions within their field both at technical and conceptual levels. The group is scientifically very robust but also develop remarkable translational research in line with their scientific findings. They are highly productive with a strong international reputation in their field. The attractiveness of this team and interactions with the non-academic are outstanding. To note the strong involvement of the team in the set-up of the state of the art (IBiSA) organoid platform of the CRCM that is an asset for the community.

Strengths and possibilities linked to the context

This team is successfully co-headed by a clinician and a scientist with complementary skills and expertise. Over the period the team has achieved outstanding contributions within their field and a major breakthrough both at technical and conceptual levels. This work led to an outstanding scientific production in PDC, without taking into account the medical/clinical publications from clinicians associated with the team. These articles have been published in the best journals including in the most prestigious one and some were widely publicised and highly cited (as examples: Nat Med 2017, Nature Commun 2021, Cell Reports 2017, Embo Mol Med 2019, and Cell 2022…). Of notice, publications in PDC are not only issued from the co-PIs but also from other senior members of the team illustrating the gathering of talents in this team. Altogether, this record confirms that the team as a whole is highly competitive at the international level in its field.
The team has developed original methodology and in-house valuable tools and models (PDXs, organoids). Team members are at the initiative of a state-of-the-art CRCM platform to generate organoides/tumoroides, with a national accreditation (IBiSA) and a leadership role in the networking of similar platforms in France, a true asset for CRCM.
The team has an outstanding funding power (different team members were PI in numerous competitive national grants – one PIA, one ANR, four INCA, one Cancer Plan, eleven charities and two industrial contracts – and they participated to seven other INCA or University grants – . The team obtained the 'labellisation' by the French LNCC 2020–2025. At national and international level, the team benefit from a large recognition in the field of mammary cancer stem cells. This led to excellent and productive collaborations. Of notice, a member of the team was PI at Indiana University and granted by this institution before she joined the team during the period.
This team has been a co-leader in structuring and promoting a national network on cancer stem cells – Sunrise network with annual meeting organisation and courses for students or professionals, involvement in the board of FSSCR –.
PIs are board members of editorial committees – Frontiers in Molecular Medicine; International Journal of Breast Cancer –. Members of the team participate in scientific committees and councils for government agencies or charities, at local, regional or national levels. They are invited to lecture in Hong Kong University and Georgia's cancer centre or meetings – Breast cancer stem cell symposium, Gordon's research conferences… –.
During the period the team trained eight doctoral students with five that defended their PhD.

Weaknesses and risks linked to the context

Despite a move to translational research and involvement at several levels in IPC's initiatives, the team is not yet involved in a clinical assay, nor has valued its research's success at the patent level.
Despite the high quality of the research and the potential of attractiveness this generates, the team did not succeed or choose to not recruit postdocs over the evaluated period, a situation that meets a general difficulty in France, and particularly in provincial areas, to attract high-level candidates for these positions. However, the panel notes that a first postdoc will join the team at the end of 2022.
The fund-raising and networking activities at the national level are remarkable, but there is room, considering the international competitiveness of the team, to improve these items at the international level, in particular at the European level – EU funding and networks as HSFP, Transcan, Mission Cancer, ITN, etc. – .
The team lacks in-house bioinformatics.

RECOMMENDATIONS TO THE TEAM

The team should put in place a strategy to recruit high-level postdocs and/or additional permanent scientist as they are now very attractive and visible at the national and international levels.
The panel also encourages the team to build on its rapidly increasing recognition in the field to extend the team network in Europe in order to access EU funding and recruitment.
The team lacks in-house bioinformatics, but this is true for other CRCM teams that should organise collective solutions to this problem.

Team 20: ATIP/AVENIR : Strand-bridging DNA damage and blood diseases

Name of the supervisor: Mr. Christophe Lachaud

THEMES OF THE TEAM

The main goal of the team is to design new tools to better understand DNA interstrand crosslinks – ICLs – -inducing agents as well as the mechanisms of repair of the lesions caused by these compounds. Within this framework, the team develops three projects:

1) The design of detectable ICL-inducing agents to monitor lesions in cells,
2) The evaluation of FAN1 protein expression levels in breast cancer as a predictive factor for resistance to anthracycline/taxane combined chemotherapy, and
3) The identification of genome integrity maintenance by UFM1 by characterising telomere integrity in UFM1-deficient cells.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was not evaluated last time being an Atip/Avenir team.

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

EVALUATION

Overall assessment of the team

The science developed by the team is very good and led to the publication of one article in an excellent journal in 2021. Its attractiveness is excellent with the obtaining of numerous grants in response to competitive calls. The team is also excellent in valorising the outcome of its research towards industrial partners. The overall assessment of the team is thus excellent.

Strengths and possibilities linked to the context

The PI was recruited at CRCM in 2016 thanks to an ATIP-Avenir grant. During the evaluation period, the team was composed of one CR CNRS (team leader), one MD, one IR1 INSERM, one IE CNRS, one postdoc and one PhD student.

The team presents a good success rate in competitive calls for proposals, as PI (ATIP-Avenir 2017-21, PIA ERC-booster 2018-20, *Fondation de France*, CR PACA 2017, 2018 and 2021) and coordinator in ANR 2019-24, demonstrating the quality and originality of its research projects. Some discoveries of the team have been patented (1 patent in 2020) or protected *via* a declaration of invention (2 declarations of invention as PI), offering the opportunity to collaborate with industrial partners (ASTRAZENECA).

The team has a good rate of publications (5 articles and 1 review over the period) and published in high rank journals as PI (1 Science Adv, 2021) and partner (1 Nucleic Acids Research, 1 Immunity, 1 Molecular Cell, 1 Trends Immunol), thus providing a high international visibility to this young team.

The team has four collaborative projects with other teams within the CRCM and initiated several collaborations with physicians at IPC. The research projects are multidisciplinary, associating the skills of biologists, pathologists, clinicians and chemists.

Since 2021, the PI participates to the editorial board of Frontiers in Cell and Developmental Biology and Scientific Report, attesting of his investment for the diffusion of science.

The PI is the coordinator of the DNA damage analysis platform and imaging platform (IMAGIN) at CRCM that includes two permanent engineers.

Weaknesses and risks linked to the context

While the publications of the PI are of a very good level, the number of publications as corresponding author is weak (1 publication for the period 2016–2021). The team, however, is still young and appears to be dependent on the patent deposition before publishing. Manuscripts are apparently ready to be submitted.

No student defended during the evaluation period.

The PI was invited to give conferences only in Marseille during the evaluation period.

RECOMMENDATIONS TO THE TEAM

Regarding the number of research projects developed by the team, the PI should have a policy for increasing its manpower, for instance by recruiting senior postdoc researchers eligible to obtain a permanent position at CNRS or INSERM.

The PI should increase the number of papers published as corresponding author.

The projects interfacing chemistry and biology should be conducted in collaboration (e.g. with teams specialised in the synthesis of organic compounds with biological activities) rather than with the platform of CRCM.

CONDUCT OF THE INTERVIEWS

Date(s)

Start: 23 novembre 2022 à 8 h 30

End: 25 novembre 2022 à 18 h 30

Interview conducted: on-site

INTERVIEW SCHEDULE

Wednesday, Nov 23
8:30 a.m. Arrival of the committee/Coffee
8:45 Presentation of the committee
9 a.m.-9:40 a.m.: Jean-Paul Borg, director of the unit: administrative and scientific presentation of the unit (20mn presentation, 20mn questions)
9:45 a.m.-10:35: Team#1 (Michel AURRAND-LIONS) Leuko/Stromal interactions in normal and pathological haematopoiesis
10:35-11:25: Team#4 (Patrick CHAMES) Antibody Therapeutics and Immunotargeting
11:25 – 12:15: Team#5: (Jean-Paul BORG) Cell polarity, Signalling and Cancer
12:15-1:05 p.m.: Team#6 (Yves COLLETTE and Xavier MORELLI) Integrative Structural and Chemical Biology
1:05 p.m.-2:05 p.m.: Lunch
2:05 p.m. – 14h:30 Break of the committee
2:30 p.m.-3:20 p.m.: Team#7 (Paulo DE SEPULVEDA and Patrice DUBREUIL) Signalling, Haematopoiesis and Mechanism of Oncogenesis
3:20 p.m.-4:10 p.m.: Team#8 (Estelle DUPREZ) Epigenetic factors in haematopoiesis
4:10 p.m.-5 p.m. Team#10 (Vincent GELI) Telomeres and Chromatin
5 p.m.-6:30 p.m. Coffee break/Debrief of the day: Unit and Teams
End of all sessions

Thursday, Nov 24
8:30 a.m.-9 a.m.: Arrival of the committee/Coffee
9:00-9:50 Team #9 (Pierre-Henri GAILLARD) Structure-Specific Endonucleases and Genome Stability
9:50-10:40: Team #20 (Christophe Lachaud) DNA Interstrand Crosslink Lesions and Blood Disorders
10:40-11:30: Team #11 (Juan IOVANNA) Pancreatic cancer
11:30-12:20: Team #12 (Bertrand LLORENTE) Genome Dynamics and Recombination
12:20-1:10 p.m. Lunch
1:10 p.m. – 13h:30 Break of the committee
1:30 p.m.-2:20 p.m.: Team #13 (Mauro MODESTI) Homologous Recombination, NHEJ and Maintenance of Genomic
2:20 p.m.-3:10 p.m.: Team #16 (Pascale ZIMMERMANN) Spatio-Temporal Regulation of Cell Signalling – Scaffolds & Phosphoinositides
3:10 p.m.-4 p.m.: Team #15 (Vincent PAGÈS) DNA damage and genome instability
4 p.m.- 4:30 p.m. Coffee break/30 min
4:30 p.m.-6:30 p.m.: Debrief of the day
End of all sessions

Friday, Nov 25
8:30 a.m.-9 a.m.: Arrival of the committee/Coffee
9:00-9:50 Team #14 (Jacques NUNÈS and Daniel OLIVE) Immunity and Cancer
9:50-10:40: Team #17 (François BERTUCCI and Émilie MAMESSIER) Predictive Oncology
10:40-11:20: Team #18 (Emmanuelle CHARAFE-JAUFFRET and Christophe GINESTIER) Epithelial stem cells and cancer
11:30-12:30: Committee split in 3 groups for closed-door discussion with:
Students (stagiaires, PhD) – Scientists (researchers not team leader, postdocs, others, …)-Managing staff (administrative and technical staff)
12:30-1:30 p.m. Lunch
1:30 p.m. – 2:30 p.m. Meeting with the managing bodies (closed doors):
Inserm: Marc Savasta (Délégation régionale) et Alain Eychene (Institut Thématique Cancer)
Hôpital : Anthony Goncalves(IPC) et Emilie Garrido (Directrice Recherche en santé)
CNRS : Aurélie Philippe (déléguée régionale) et Yvan De Launoit (en visio, INSB)
Université AMU : Philippe Laporte (VP recherche)

2:30 p.m.-2:45 p.m. Coffee break: Private meeting of the visiting committee (in presence of the HCERES scientific advisor)
2:45 p.m.-3:30 p.m.: Discussion with the director + deputy (closed doors)
3:30 p.m.-18–30: Committee final debriefing.
6:30 p.m.
End of the visit

PARTICULAR POINT TO BE MENTIONNED

NA

GENERAL OBSERVATIONS OF THE SUPERVISORS

Le Président de l'université

au

Département d'Évaluation de la recherche - Hcéres

Objet : Observations de l'unité relatives au rapport d'évaluation des experts Hcéres

N/Réf. : VPR/LS/AMS/CM – 23-07

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

Vos réf :
DER-PUR230023051 - CRCM - Centre de recherche en cancérologie de Marseille

Marseille, le vendredi 14 avril 2023

Madame, Monsieur,

Je fais suite au mail que vous nous avez adressé le 16/02/2023 dans lequel vous me communiquiez le rapport d'évaluation Hcéres de l'Unité CRCM - Centre de recherche en cancérologie de Marseille.

Comme demandé dans ledit mail, je vous fais part ci-après des observations de portée générale de l'unité:

The management and all the CRCM teams would like to thank the HCERES committee for its very important analysis work and its very constructive comments.

We are particularly satisfied with the overall evaluation, which places CRCM between excellent and outstanding, and we thank the committee for its recommendations aimed at making us progress further.

However, we would like to make a clarification concerning the evaluation of domain 2 (Attractiveness), which notes that the proportion of publications signed by PhDs students as a proportion of the total number of CRCM publications is very low (17%). As part of the very close partnership between the CRCM and the IPC, 5 CRCM teams include clinician-researchers who also carry out purely clinical research studies (=708 clinical publications out of the 2646 articles counted in the period 2016-2021). These articles do not lead to the involvement of PhDs, with the exception of the COMPO team, which works specifically on the mathematical modelling of these studies. At the level of the CRCM teams, we obtain rates of signatures of articles by students varying from 14 to 57%, which seem to us to better reflect this specificity.

Team 1: Leuko/Stromal Interactions in normal and pathological haematopoiesis
Name of the supervisor: Mr Michel AURRAND-LIONS

The committee mentioned the limited manpower of the team due to the departure of one PI with a permanent position and the need to put in place a strategy to recruit postdoc eligible for CRCN recruitment.
Cyril Fauriat, CRCN INSERM, joined my team in 2021 after the departure of S. Mancini in 2020. Two new members will join my team by the end of 2023: Véronique Gelsi-Boyer, PU-PH and Nathalie Cervera, part-time engineer. I think that these arrivals will compensate the departure of S. Mancini.
Concerning the second recommendation to limit research axes: I will definitively stop working on B-acute lymphoblastic leukemia (B-ALL) to focus on myeloid diseases which is also the research focus of the new incomers. This is described in the 2024-2028 project of my team.
Finally, I will stop animal facility management, but will not stop my involvement in experimental histopathology platform management as recommended unless this is taken over by a member of my team. I believe that strategic decisions regarding new technologies available on platform are essential. This is made possible only if the person in charge of the platform is also beta-tester of the new technologies before making them available for other teams. The strong involvement of my team in technological developments (especially single-cell) is recognized as a strength by the HCERES committee. We currently set-up spatial transcriptomics and multiplex fluorescence imaging (MacSima) in my laboratory in order to transfer these technologies to the experimental pathology platform.

Team 4: Antibody Therapeutics and Immuno-targeting
Name of the supervisor: Mr Patrick CHAMES

Weaknesses and risks linked to the context
The team has no European or international funding that would allow them to be more attractive for international postdocs and to recruit them.
- We actually have an international funding (ANRi Nanovir) running since 2021.
- We are also applying this year for the second time to a European EIC Pathfinder Open call.

Although the team and its PI are well recognised in the nanobody field, they have not been involved in the organisation of national or international meetings.
- To improve this issue, we have applied for a funding to organize an international "Nanobodies worshop" in 2024. Our proposition has already been shortlisted.

RECOMMENDATIONS TO THE TEAM
As the manpower of the team is limited, the team should put in place a strategy to attract postdocs eligible for CRCN recruitment.
The team will be reinforced in august 2022 by the arrival of Rémi Lasserre (fundamental Immunologist, CRCN INSERM), currently working at CIML, Marseille.

The team should initiate more mechanistic studies that may be published in prestigious journals.
- This issue should indeed be improved with the arrival of Dr Lasserre, specialist in fundamental studies of T cell activation and signaling.

***It is also recommended to favour collaborations with other CRCM teams which could bring their expertise in immune checkpoint therapies, preclinical models and clinical trials*.**
We have recently initiated two inter-CRCM department collaboration (Borg team and Zimmermann team), and we have been involved in two large collaborative proposals (SIRIC MiSTRal (integrated research program 2, new therapies, project 4) and IHU OverCancer (WP2, Development of Novel Therapeutics).

Team 9: Structure-Specific Endonucleases and genome Stability (Pierre-Henri GAILLARD)

A few errors would need to be corrected in the report.

It is mentioned in a couple of instances that we have a program related to paediatric leukemia (points **1** and **4** below). This is not the case.

I have been a coordinator on all our grants over the last 10 years including both the INCA PLBIO 2017 and 2019 grants. "The team was successful in grant funding during the complete period one INCa PLBIO as coordinator in 2017 and 2019. The team received the prestigious label 'Équipe FRM' from the foundation as a single team in 2021."

Team 16: Spatio-Temporal Regulation of Cell Signalling – Scaffolds & Phosphoinositides
Name of the supervisor: Mrs Pascale ZIMMERMANN

The committee mentioned as weaknesses and risks linked to the context taht: *" Although a MCU recently joined the team, it is of very small size and no indication appears related to the recruitment of researchers. At the level of the team, training through research is very low in terms of students and postdoctoral fellows (3 PI and 1 postdoc).*

RECOMMENDATIONS TO THE TEAM The strengthening of manpower must be pursued in order to stabilise and develop the main projects

There are not 3 PIs in my team over the period 2016-2021, but at most 1.5 : Guido DAVID (0.5) and myself (1), the only one with an HDR. I think that given this situation, we have actually educated quite a few students (about 15), see attached table (period 2016-2021, knowing also that most of them have found a job or continue their studies).

However, I agree that the team needs to be strengthened, and I have already done so, since the team has been reinforced by the arrival of Sylvie THUAULT (MCU AMU - Molecular Biology and Cancer Cell Biology, 50%) and, since March, of a new post-doc (Cristobal CERDA-TRONCOSO - Molecular Biology and Cancer Cell Biology, KU LEUVEN), see the organisation chart below.

Pascale ZIMMERMANN IPC - DR 2 INSERM - KU LEUVEN - PI
Guido DAVID EM PROF (50%)
Rania GHOSSOUB* IR AMU - Cell Biology
Sylvie THUAULT* MCU AMU - Molecular Biology and Cancer Cell Biology (50%)
Raphael LEBLANC* POST-DOC IPC - Cancer Biology
Salomé DUSSERT* IE INSERM - Molecular Tools
Marie HUBER* PHD AMU - Molecular Biology and Cancer Cell Biology
Lukas HYKA PHD FWO - Therapeutic EVs
Sofie MEUSSEN IE FWO-KOTK - Therapeutic EVs
Félix REY-CADILHAC joined PHD UMontpellier vaccine against mosquito EVs
Michiel DECOSTER joined PHD FWO VUB Multiple myeloma therapeutic EVs
Chenggong TU joined PHD CST VUB Syndecan/CD138-syntenin EV exchanges in Myeloma
* full-time at CRCMarseille

Team 20: DNA interstrand crosslink and blood disorder (**Mr Christophe LACHAUD)**

The committee recommended to increase manpower of the team to match the numbers of research project by recruiting senior postdoc eligible for CRCN recruitment : In 2019, I submitted a senior researcher with whom we collaborated, Dr Ana Belen Perez-Oliva, to the competition. Unfortunately, she was not ranked high enough to get a position and she is now a group leader in Spain. Since January 2023, we have recruited a senior postdoc to the laboratory and we have obtained European funding for two other senior researchers. We expect them to apply for permanent research position. I have also turned to a different strategy of recruiting an INSERM researchers (CRCN) who was looking for mobility, Dr. Jean-Hugues Guervilly. He joined the laboratory in 05/2022. Finally, I would like to highlight the presence of a doctor in the laboratory, Dr. Yosr Hicheri, who since 01/2021 is in charge of the supervision of interns and translational. I think that these arrivals will make the number of projects more manageable.

Concerning the number of publication as a PI that should be increased and the absence of PhD student: Like all groups we have been impacted by the covid crisis but I believe, the impact for a young group (only 2 years existence) was massive. First of all, this has delayed by a year the defense of our student by a year (06/2022). Then it has impacted the project of 2 postdocs who were unable to finish their work due to contract finishing during covid and not extended. We have now hired the postdoc to finish the projects. Finally, has mentioned by the experts, one of our key projects was under embargo due to patent deposition. The paper has been submitted to Nucleic acid research and received very positive feedbacks. It will be resubmitted when requested experiment are achieved. Our strategy of patenting appeared to be good since, with the support of INSERM Transfer, we are now in the process of setting up a startup with a CEO we identified.

Concerning the invitation of the PI to conferences limited to Marseille: I have not been invited to international meeting since 2016. However, my invitation to conferences were not limited to Marseille. CHO DINGO and 3R meeting are national meetings that have been organized in Marseille or in Giens (a city 2 hours away from Marseille).

Finally, for the collaboration with chemist instead of the use of the chemistry facility: I have been in contact with the Pr. Bonnet (Univ of Orlean) for the collaboration in chemistry. We submitted an INCA together but it has not been selected for funding. We will further explore the possibility to collaborate with teams specialized in the synthesis of organic compounds.

Vous souhaitant bonne réception des présentes,

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

Eric BERTON

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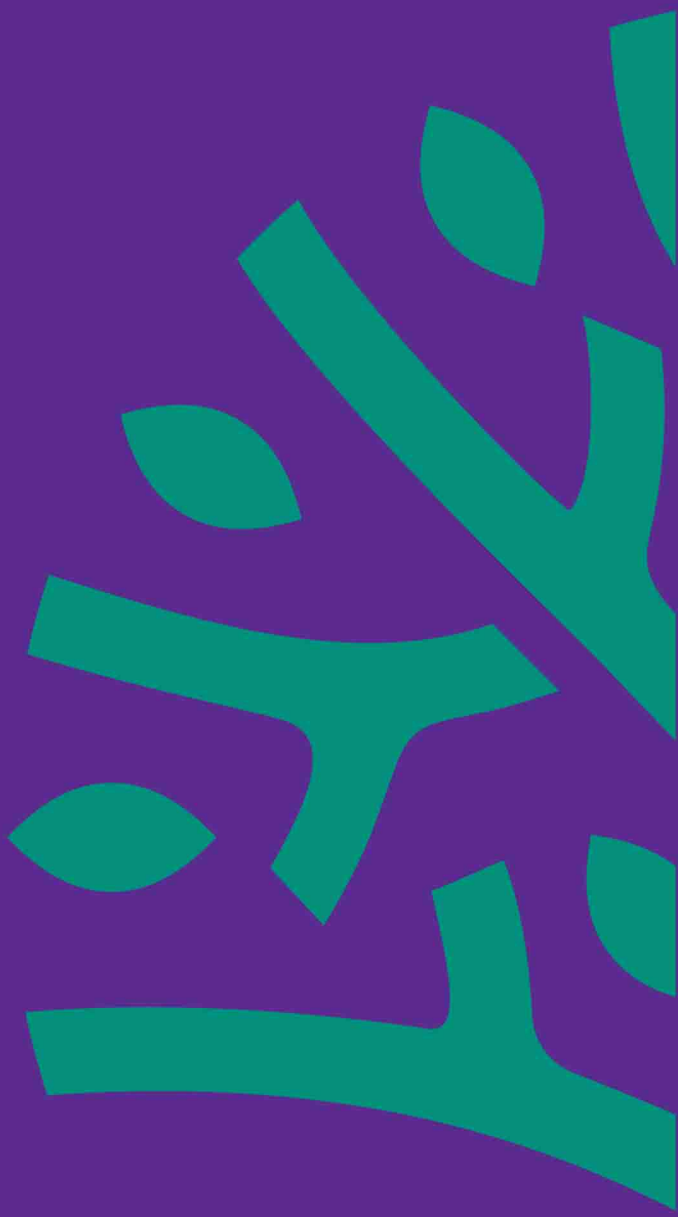

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