Research evaluation

EVALUATION REPORT OF THE UNIT

CIML - Centre d'Immunologie de Marseille-Luminy

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Aix-Marseille université - AMU

Centre national de la recherche scientifique - CNRS

Institut national de la santé et de la recherche médicale - INSERM

EVALUATION CAMPAIGN 2022-2023

GROUP C

Report published on June, 21 2023

High Council for evaluation of research and higher education

In the name of the expert committee[1] :

Stefano Casola, Chairman 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: Mr Stefano Casola, The FIRC Institute of Molecular Oncology, Italy

Experts:
Ms Nelly Bonilla, Inserm, Paris (supporting personnel)
Ms Francesca Chiodi, Karolinska Institutet, Sweden
Ms Rima Haddad, Université Paris Saclay (representative of CNU)
Mr Sebastien Lacroix-Desmazes, Inserm, Paris
Ms Nicole Pavio, Anses, Maisons-Alfort
Mr Michael Schindler, Tübingen University Hospital, Germany
Ms Nabila Seddiki, CEA, Fontenay-aux-Roses
Mr Jean-Claude Sirard, Inserm, (representative of CSS Inserm)
Mr Peter Van Endert, Université Paris Descartes
Mr Joost van Meerwijk, Université Toulouse 3 (representative of CoNRS)

HCÉRES REPRESENTATIVE

Mr Jacques Dutrieux

CHARACTERISATION OF THE UNIT

- Name: Centre d'Immunologie de Marseille Luminy
- Acronym: CIML
- Label and number: CNRS UMR 7280 - Inserm U1104 - AMU UM 2
- Number of teams: 18
- Composition of the executive team: Mr Philippe Pierre

SCIENTIFIC PANELS OF THE UNIT

SVE4 Immunité, infection et immunothérapie

THEMES OF THE UNIT

The Centre d'Immunologie de Marseille Luminy (CIML) is a pluri-thematic unit consisting of around 180-210 units of personnel, of which 58 hold permanent positions (distributed among professors, senior scientists and research supporting personnel). The unit is divided into 18 research teams which address a wide variety of topics related to immune cell ontogenesis, adaptive and innate immune responses, and immune-cell associated disorders including lymphomas. The unit teams take advantage of a unique set of transversal technological platforms developed over the years and continuously enriched with state-of-the art new technologies, ranging from preclinical models, to advanced imaging, (single cell) genomics, cytometry, histology and bioinformatics. Team leaders constitute a well-balanced mixture of senior and junior principal investigators leading mid-large size research groups and scientifically contributing to the establishment and coordination of core technological platforms. CIML reputation as center of excellence for immunology research goes hand-in-hand with an interest of several teams to transfer basic knowledge into the clinical setting with the ultimate goal to understand better disease pathogenesis as well as identify new therapies to combat immune disorders and cancer. The drive to increase international visibility has led CIML investigator to establish scientific alliances with research institutes in foreign countries and create a relationship with the EMBL.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The Centre d'Immunologie de Marseille Luminy (CIML), was originally established in 1976 by CNRS, in collaboration with Inserm, the Aix-Marseille University (AMU), the Fondation pour la Recherche sur le cancer, the city of Marseille, the Bouches du Rhône department and the Provence-Alpes-Côte d'Azur region. The unit is placed within a multi-disciplinary campus in the Aix-Marseille metropole. The location hosts 2 faculties, 32 research laboratories, biotechnology companies including some budding of from CIML discoveries. The unit is currently directed by Dr Philippe Pierre, and benefits from independent administrative and informatics service which support the daily research activities of 18 independent teams.

RESEARCH ENVIRONMENT OF THE UNIT

CIML is a research unit located in the Luminy campus Aix-Marseille Metropole, established thanks to a collaboration between Inserm, CNRS and the Aix-Marseille University (AMU) and the support of the Fondation pour la Recherche sur le Cancer and local and provincial authorities. CIML advanced expertise in imaging led to the unit's recognition at the national level as "Infrastructure en Biologie Santé et Agronomie (IBISA)" and is a member of the France Bioimaging (FBI) network, a national infrastructure, which received the nomination as "Programme d'Investissements d'Avenir (PIA)".
A total of eight CIML teams have participated between 2014 and 2020 to two Laboratory of scientific excellence (labex) initiatives. Ongoing local networking initiatives to which CIML is participating through the representation of its teams include the "Institut de Convergence CenTuri", an interdisciplinary initiative bringing together experts in biology, physics, mathematics, computer sciences and engineering to unravel the complexity of living systems. Through the Aix-Marseille Initiative of Excellence (AMidex), CIML received Chairs of excellence for three of its team leaders. To foster collaborations with clinicians, CIML contributed to the creation of the Institute of Cancerology and Immunology (ICI) which was sponsored by AMidex Foundation and the AMU. Thanks to an initiative promoted by Dr E. Vivier within the Hôpitaux de Marseille, CIML also benefits from the Marseille-Immunopole (MI) cluster and immunoprofiling platform (MI-PP), which ensures access to patient material and clinical resources. Through the MI, CIML was linked to University-Hospital Federation, a clinical institute dedicated to precision immuno-oncology, which allowed two CIML members to contribute to the RHU "Pioneer Project" focused on mechanisms of cancer resistance to PD-1(L) checkpoint blockade. CIML contributed to establishment of MimAbs an R&D platform for the development and characterization of immunotherapy antibodies.

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

Permanent personnel in active employment	
Professors and associate professors	4
Lecturer and associate lecturer	7
Senior scientist (Directeur de recherche, DR) and associate	20
Scientist (Chargé de recherche, CR) and associate	24
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	45
Subtotal permanent personnel in active employment	**100**
Non-permanent teacher-researchers, researchers and associates	5
Non-permanent research supporting personnel (PAR)	32
Post-docs	20
PhD Students	47
Subtotal non-permanent personnel	**104**
Total	**204**

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

Employer	**EC**	**C**	**PAR**
CNRS	0	25	18
Inserm	0	19	21
Aix-Marseille Université	11	0	6
Total	**11**	**44**	**45**

UNIT BUDGET

Recurrent budget excluding wage bill allocated by parent institutions (total over 6 years)	9 631
Own resources obtained from regional calls for projects (total over 6 years of sums obtained from AAP idex, i-site, CPER, territorial authorities, etc.)	4 532
Own resources obtained from national calls for projects (total over 6 years of sums obtained on AAP ONR, PIA, ANR, FRM, INCa, etc.)	22 457
Own resources obtained from international call for projects (total over 6 years of sums obtained)	14 146
Own resources issued from the valorisation, transfer and industrial collaboration (total over 6 years of sums obtained through contracts, patents, service activities, services, etc.)	5 309
Total in euros (k€)	46 596

GLOBAL ASSESSMENT

The global performance of the CIML unit is outstanding.
CIML has continued in the last mandate to achieve outstanding scientific production, publishing highly original research articles in prestigious journals in fields of cellular and molecular immunology, infectious disease, cancer biology and treatment. The unit has addressed previous recommendations hiring in the past mandate five new junior team leaders, who have already shown strong potential to become future leading scientists in their fields of interest through publications in prestigious journals and by securing generous funding, including two starting grants from the European Research Council. The hiring of the new team leaders was achieved through two open international calls, satisfying criteria of transparency, gender balance and excellence for the selection of candidates with the most original projects. CIML fosters intramural collaborations and has established strong collaborative networks both nationally and worldwide. Research activities are guaranteed by outstanding funding secured from national and international public and private funding bodies (including an impressive list of 6 European Research Council grants). CIML is supported by state-of-the-art technological platforms, including high-level imaging technology and latest ones centered around single-cell transcriptomics and genome wide CRISPR/Cas9 genetic screenings as well as the C2BM bioinformatics platform. CIML confirms its outstanding status in immunological research based on elegant and advanced genetically-engineered preclinical models addressing questions related to ontogeny, function and disorders of the immune system, with a recent emphasis given to neuroimmunology. Basic research addressing fundamental questions in immunology is balanced by expanding translational studies centered on the pathogenesis of lymphomas and exploitation of innate lymphoid cells for the treatment of solid and hematological cancers. Several CIML teams have established connections to the socio-economic world, including the filing of several patents and the establishment of productive partnerships with the industrial sector. CIML remains an excellent center for doctoral and post-doctoral training. Particularly the participation of CIML to the creation of the Institute of Cancerology and Immunology and its links to the "Institut de Convergence CenTuri", provide teaching opportunities within integrated programs at Master and PhD levels and development of interdisciplinary research. CIML members have strong name recognition in their respective fields of interest, receiving recurrently invitations as speakers to international meetings, participating to editorial boards of peer-reviewed scientific journals, contributing to science assessment as scientific members of national and international funding bodies, and receiving prizes for their outstanding contributions to science. CIML has invested substantial resources in the development of the C2BM core bioinformatics platform, which provides a fundamental support to the increasing demands of CIML scientists for highly qualified bioinformatics analyses and mathematical modelling.
CIML is facing a substantial restructuring of its teams, which will be completed within 2023. The impact of several CIML teams closing, restructuring or relocating will establish a new order within CIML. To what extent the reshuffling of many teams will impact on the careers of permanent researchers, graduate students, engineers and technicians involved in these movements is presently difficult to estimate, and represents an aspect of the future unit's life. The new scientific direction will need to assess this with great care. In support of this, a higher transparency of decision making processes and improvement of top-down communication to the personnel (researchers, engineers, and technicians) is encouraged. Closer mentoring by the scientific direction and team leaders, of permanent staff (researchers, engineers, technicians) for timely planning of suitable career paths, together with offering a stronger visibility to, and care for lab personnel needs is expected to improve the Unit's spirit. Revising and optimizing the administrative support for non-French-speaking researchers will help to further increase the excellent international visibility CIML has, contributing to attract more foreign researchers.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

1. Mid-long term vision for CIML: During the last evaluation period, the Scientific Direction has promoted a wave of new hirings. The appointed five junior team leaders have already proven their potential securing highly competitive/prestigious starting research grants.
2. Institutional cohesion: CIML organizes regular scientific and social retreats to improve the "esprit de corps".
3. International attractiveness:
i. For the evaluated period, CIML hosted 35 PhD students and 40 post-doctoral fellows from abroad.
ii. The unit has established in 2019 of a CNRS International Research laboratory as part of an alliance with the Shanghai Institute of immunology.
iii. In 2020 CIML has signed of a memorandum of understanding with EMBL to sustain joint research projects and strengthen the link between CIML and the wider EMBL community.
iiii. Through AMU, CIML benefits from the EU-funded "CIVIS" post-doctoral program.
4. Acknowledgment of staff members of core facilities: CIML teams regularly include staff members of core facilities in the author list or acknowledgements of their publications.
5. Funding opportunities for early career scientists: Recently hired junior group leaders and junior scientists have secured funding from independent national and international agencies (ERC, ANR, ATIP/Avenir).
6. Intramural communication: Decisions reached within the council of team leaders are communicated on the same day to the Laboratory council, which includes all staff representatives. Minutes of the meetings are publicly available.
Starting from 2020, each staff category meets in multiple occasions with the scientific direction to improve organization and life of CIML. The action was completed by a global survey on the well being of the the staff which was performed by Inserm.
Social events, scientific retreats and participation to public events highlighted unit's achievements are expected to improve communication between the scientific direction, team leaders, researchers of their unit and staff personnel of all categories.
7. Training programs and mentorship: Recommendations to improve the structuring of graduate programs active in CIML and mentorship of graduate students could not be addressed as they refer to rules and regulations of the local doctorate program.
CIM has implemented a meeting between 1st year PhD students and the scientific director to address/prevent potential issues arising from the student/mentor relationship.
8. New technologies: CIML invested in the last evaluation period in the setup of a platform of single-cell transcriptomics and in the possibility to perform CrispR/Cas9 genetic screenings.
The participation of CIML to local clinical initiatives including ICI and MI-PP is expected to substantially strengthen the connection between basic research held in CIML and clinical activities in particular in the field of immunooncology and Covid19-related disorders.

B – EVALUATION AREAS

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

Assessment on the unit's resources

CIML scientists globally have access to outstanding resources. This includes free in-house and additional outside core facilities, excellent third-party funding, efficient interaction with medical institutions providing opportunities for translational research and with private companies, and implication in several undergraduate programs attracting students to CIML.
However, CIML faces a risk to the level of excellence of its functioning and specifically core facilities, due to rising costs, only partly appropriate calls for equipment replacement and partial replacement of departing staff.

Assessment on the scientific objectives of the unit

The scientific objectives of the unit are excellent. CIML is integrated overall very well in the research community and has excellent networking activities. It fosters and promotes interactions with the non-academic world and has a sound strategic organization that aligns excellently with the objectives of the stakeholders.

Assessment on the functioning of the unit

The research center is very well organized. It includes outstanding State of the Art Technology Platform. The bioinformatics platform is very active in intervening at all stages of projects, from conception to final analyses. It has planned a solid data management plan. The unit organizes regular meetings with Team leaders and other scientific and engineering/technical staff. Measures were taken to correct the gender imbalance. The unit include strong team leaders in terms of capacity to raise European and national grants, and of outstanding publications and scientific visibility Worldwide.

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

Strengths and possibilities linked to the context

The unit defines itself several missions: science, technology, education, clinical and private company partnering, and academic appeal and collaboration. As all 18 teams are directed by full-time researchers, the first mission naturally dominates the activity of the teams, with a minimum of 50% of time but more representative 70 to 90% of time devoted to research and research supervision. Most teams have few (1 to 3) tenured scientists and only 6 teams between 4 and 6 permanent scientists; the intra-team technical support is fairly evenly attributed to small and larger teams, no single team has more than 1 permanent engineer/technician. Thus, research productivity relies mainly on non-permanent researchers and engineers/technicians who are numerous in many teams. This setup enables the teams to achieve a significant scientific production covering a wide diversity of subjects related to the principles governing the immune system. This production can be characterized as excellent to outstanding to exceptional, depending on the team considered.
In the context of its mission of education, CIML hosts students in the single-track master program of the Aix-Marseille-University (AMU). Other students enrolled in the recent ICI (Institute of Cancer Immunology) program focusing on immunology and oncology are also trained. Finally, CIML participates in the CENTURI Institute teaching immunology students in disciplines such as physics and chemistry.
CIML links with its Spinoff companies Innate Pharma & Ipsogen, partners with Sanofi & Medimmune, and has set up a team of scientists focusing on international relations, intellectual property management and tech transfer.
CIML develops translational activities through its leadership in "Marseille Immunopole", bringing together AMU, Marseille hospitals (AP-HM) and, at the national level, AVIESAN. "Immunopole" focuses on antibody and cell therapy for cancer and inflammatory diseases. CIML is implicated in the RHU (Réseau hospitalo-universitaire) Pioneer and partners with the regional Canceropôle PACA.
CIML is involved in numerous international collaborations, including two CNRS laboratories involving the University of Aveiro and the Shanghai Institute of Immunology, and was involved in an Inserm/Helmholtz association project.
CIML receives about 28% of the yearly budget of about 5.4 M€, excluding salaries, from its supervisory authorities. CIML has adopted the relatively uncommon model of supporting with this budget not only common expenses, infrastructure and administrative services, but also to make access and use of its seven core facilities cost are partially supported by the common budget of the institute. This model renders CIML particularly attractive for young start-up groups unable to support high core facility expenses. As another result, expenses for consumables must be covered by grants acquired by the teams. CIML teams obtained an average of 32 grants (public or private sources) per year during the period. Remarkably, ten European Research Council grants were obtained. Overheads of the latter are used to support common expenses and core facilities. CIML employs two grant officers helping with administrative and financial grant issues and reporting.
Six CIML core facilities obtained refurbished space during the evaluation period. CIML also created a new single cell genomics facility and a new computational Biology Hub. Next to its own core facilities, CIML participates in the IBISA-labelled Marseille Proteomics platform and in the CENTURI Platform with 6 engineers with expertise in physics or chemistry. Finally, CIML benefits from proximity to the Center for Immunophenomics, a public pay-for-

service facility generating gene-modified preclinical models and offering comprehensive of immune cell populations via multiplex mass cytometry.

Weaknesses and risks linked to the context

Although CIML has set up a committee monitoring (next to international relations) issues related to intellectual property and technology transfer, it is unclear whether researchers have all the competence required for identifying and managing these issues on their own.
The high standards of the services provided by CIML core facilities and administrative services depend critically on sufficient funds for equipment purchase and maintenance and for qualified personnel. As underlined by CIML leaders, the ever rising cost of new equipment replacing outdated machines, the absence of national calls providing the full cost of such equipment, and the only partial replacement of departing personnel represent a significant risk for the functioning of CIML and its level of excellence.

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

Strengths and possibilities linked to the context

CIML performs research on all levels of immunology, from basic research to applied immunology in terms of immunotherapeutic applications. For this, there is a high need to foster interdisciplinary research and to integrate into various networks and clusters. CIML is excellently integrated and continuously strives to establish novel collaborations and networking activities. Ample examples are detailed below.
CIML has ongoing collaborations at the Luminy campus in detail the Laboratory of scientific excellence (Labex), the Labex DC-Biol together with the Institute Curie and the University of Paris-Sorbonne. The collaboration with the Labex INFORM with the Institute for Development Biology (IBDM) and Aix-Marseille Unviersity was terminated in 2020 by Aix-Marseille University. CIML is further involved in the "Institute Convergence CenTuri", aiming to understand how biological function emerges from the organization and dynamics of living systems (https://centuri-livingsystems.org). CenTuri is one of 20 multidisciplinary research institutes of the Marseille area.
CIML benefits from the Aix-Marseille-University Idex (AMidex), receiving three Chairs of Excellence for new group leaders and other competitive grants including an International Research Laboratory together with the University of Aveiro, Portugal.
CIML participated in the creation of a novel Institute of Cancerology and Immunology (ICI) sponsored AMidex Foundation which is a structure aiming to integrate key research topics for AMU. This promotes integration of basic and clinical immuno-oncology research and facilitates students recruitment, basic-to-clinical research and hence valorization of results. Furthermore, CIML integrates into the Marseille-Immunopole cluster and immunoprofiling Platform (MI-PP) within the Hôpitaux de Marseille (AP-HM) to foster clinical and bench-to-bedside research. Through this cluster, CIML is associated to the clinical institute MI-FHU in 2015 and thereby to the RHU "Pioneer Project" for Precision Immuno-Oncology for advanced Non-Small Cell Lung and Cancer Patients with PD1(L1) ICI Resistance.
CIML was one of the founders of MImAbs (https://www.mimabs.org), an R&D Platform for the generation and characterization of immunotherapy antibodies. MImAbs was originally an industrial demonstrator financed by the PIA program and was transformed as an independent company in December 2020.
CIML is a large unit with 18 teams (14 teams by 2024) and during the years developed several committees as well as a Scientific Advisory Board to discuss the strategy on the unit and implement it into its research vision and networking activity. There is active participation of group leaders in the committees but also researchers and technical staff. The internal organization and how it is translated into operational implementation is mainly influenced by the recruitment policy, as team leaders independently follow on their research topics. This has proven successful throughout the years.
Two CIML teams are part of the strategic positioning of the Carnot Network [through CALYM endorsement] in "*France Relance*" through the "Plan Innovation Santé 2030" from the Research ministry (MESRI) to develop French Tech, and stimulate private/public partnership in biomedical innovation. At the societal level, several Teams are involved into the translation of their research into clinical development (mainly early clinical trials). In the evaluation period there was 1 biotech created and 24 patents filled, which is excellent.

Weaknesses and risks linked to the context

While CIML has started to foster interactions with non-academic institutions, it is still somehow lacking strong interactions with clinical partners. Furthermore, networking activities are mainly driven by few well established team leaders and there seems to be no overall strategy of the unit's direction to establish a CIML headed immunological research hub at the local or national level, as it might be appropriate for the leading French institute in all areas of immunology. It is unclear how the engagement into the Carnot Institute is supposed to contribute to the institute's revenues.

Furthermore, while there is a decent amount of patents, the question is if there is a clear roadmap to promote licensing and valorization of patents in terms of an ongoing tech-transfer management.

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 CIML complies in human resources management according to the institutional rules of the employers (CNRS, Inserm, AMU). The gender equality is mainly supported by a task force cell, information meeting and exhibition with an association.
The unit appointed 3 "*assistant de prevention*" to guarantee training and information to users with regard to chemical and biological manipulations. Of note, a welcome day is organized to introduce all the safety rules for new comers. Interestingly, the new comers have also a presentation and a visit of the CIML core facilities to facilitate any future interactions in their work.
Regarding risk associated to stress, the CIML has set up a survey with the institutions and the results were highly encouraging after the lockdown period since the personnel were rather comfortable with the actions conducted by CIML and no major outputs in terms of mental distress was noted.
CIML is very well-structured regarding the protection of its scientific assets and computer systems.
The Unit is engaged in sustainable development and has encouraged recycling and bike transportation by providing parking, repair services and bins for paper, plastics, tip box recycling.
The CIML has set up a Business Continuity Plan (BCP) to cope with CoVID-19 context. The BCP can be activated at any time if required.

Weaknesses and risks linked to the context

The number of "*assistant de prevention*" is relatively low with regard to the number of personnel, especially the short-mid-term contracts that constitute 50% of the human resources.
Interviews with the non-leading scientific staff and with the technical/engineering staffs independently pointed out some degree of frustration in terms of recognition. The technical staff expressed lack of, or minimal, support from some team leaders and/or from the direction for their personal carrier development plans.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The attractiveness of the unit is excellent. The members of the unit are strongly recognized for their major scientific contributions in the fields of fundamental and applied immunology, and cancer biology. CIML is a very attractive structure for students and post-docs interested in advanced training in immunology and for young researchers who wish to pursue their own research programs. Outstanding fund raising capacity, with state-of-the-art technological platforms greatly contribute to CIML attractiveness.

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

During the reference period, team-leaders and staff-scientists of the CIML were invited to orally present their data to almost 500 congresses, symposia, and academic institutions worldwide. These conferences were given at prestigious institutions such as Keystone conferences, Harvard University, EMBL, the Francis Crick Institute, Shanghai University, etc. They also participated to the organization of more than 30 (inter)national symposia and congresses and of a monthly educational and scientific webinar. Many CIML members hold editorial responsibilities in scientific journals (ex. *Frontiers*, *J Exp Med, Immunity, EMBO J*) and sit in scientific expertise bodies in France and abroad (e.g. FRM, ARC, ERC, CNRS, Inserm, Hcéres, INCa, ANRWellcome Trust, Riken Institute, Weissmann Institute, etc.). Five CIML members are elected or appointed members of national and/or international scientific academies (e.g. EMBO, Académie de Médecine, Académie des Sciences, American academy of microbiology). More than ten CIML members were laureates of prestigious prizes (e.g. Grand prix

de la FRM, Médaille d'argent and médaille de bronze of the CNRS). These observations demonstrate an outstanding scientific reputation of the CIML.

Weaknesses and risks linked to the context

No weakness identified.

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

Strengths and possibilities linked to the context

Since 2016, the CIML has integrated 5 new teams, 3 of which are led by new researchers. The latter are among the 10 researchers recruited during this period.
During these 6 years, the CIML has also welcomed 73 post-doctoral fellows.
For the evaluated period 2 researchers were hosted: one hosted by the Pierre Team and another one, in Vivier Team.
The CIML has an organization for the reception of PhD students and post-doctoral fellows that seems to be well in place at different levels.
For the newcomers, a visit of the technological platforms is planned with a training leading to autonomy according to the needs.
The supervision of PhD students includes a sponsor who supervises the progress of projects and a mid-thesis progress report. One week per year is reserved for the presentation of 1st year students' topics as well as conferences with experienced researchers.
Assistance is also provided to foreign fellows with technical and financial support for their research as well as French language courses.
There is also financial support for students wishing to visit a Harvard-affiliated laboratory.
The CIML also sponsors newcomers to the Marseille Metropole to obtain an installation grant.
The organization of social events, not all of them scientific, allows to create a link and a team spirit for all the CIML staff.

Weaknesses and risks linked to the context

Half of the ITAs are non-statutory and this is a weak point in the lab's memory.
After discussion with the different categories of staff, there seems to be a feeling of lack of recognition in some teams.

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

CIML teams finance their research activities and hire researchers through a huge number of external very competitive funding. They have an outstanding capacity to raise funds from European or national institutions, public or charities reaching about 7 700 k€/year of own resources.
At the European level, over the reference period considered (2016-2021), 4 teams have obtained an ERC contract (>7 000 k€) including one new team leader (ERC starting grant), 5 teams have benefited from other European funds such as Proof Of Concept (150 k€) and Maria Slodowska-Curie (>800 k€), among which 2 young investigator teams. In addition, the CIML leads collaborative and multidisciplinary projects with a team involved in a Future Emerging Technologies Open funding (>460 k€).
At the national level, the CIML has benefited from a large number of diversified funding opportunities, testifying the remarkable interaction dynamics between the different core activities of the research teams and the scientific and societal programs of interest led by public or associative organizations.

Over the evaluated period, 12 teams (i.e. more than half of the research entities), including 2 young investigator teams starting during the current mandate, were awarded 21 ANR grants (>7 000 k€) as coordinators and 6 teams were partners in 10 contracts (~ 2 000 k€). The local institutional environment represented by the University of Aix Marseille Idex (AMidex), constitutes a considerable leverage. This academic opportunity, which was reflected in the previous mandate by a fruitful rapprochement between AMidex and the CIML through a Chair of Excellence, financially reinforced in 2016, and an "International Laboratory Grant" (2015-2016), has enabled AMidex to consolidate its partnership with the CIML and to invest in new Chairs of Excellence programs designed to support 3 new teams and including a PI salary. INCa was a major funding organization for 6 supporting teams (>2 600 k€) and 6 partner teams (~ 470 k€). CIML teams were also holders of contracts from ANRS (~ 270 k€), CNRS (~ 280 k€) and Inserm with 1 ATIP/Avenir program (270 k€) and 6 ITMO (~ 1 450 k€). Funds from Inserm-

Transfert (175 k€) and the Société d'Accélération de Transfert de Technologies (SATT) (>770 k€) also contributed to the economic vitality of the research structure.
The CIML has taken advantage of the Fédération Hospitalo-Universitaire Marseille-Immunopôle (MI-FHU), created in 2015, to involve 2 teams in 3 Recherche Hospitalo-Universitaire (RHU) "Pioneer Project" of the ANR-PIA projects (>1 400 k€).
In parallel to local and national financial support programs, the CIML has also seized territorial financial opportunities and has benefited from funds from the Cancéropôle PACA and more widely from the PACA and Ile de France regions (>1 200 k€).
The CIML has obtained 8 new team accreditations from charities (ARC, FRM and LNCC) and 24 new contracts from these institutions. Other private grants (ARTHRITIS, FRC, BMS Foundation, GEFLUC, MMA, MSDAVENIR, Nutricia Research Foundation, Princess Grace of Monaco Foundation, Société Française de Rhumatologie) have largely added to the structure's budget.
It should be noted that some important funds starting just at the end of 2015 significantly contributed to the functioning of 5 CIML teams for all or part of the evaluated period: ERC (~ 2 400 k€), ANR (400 k€), Inserm ITMO Cancer (250 k€ and 400 k€) and FRM (300 k€) and that one new team obtained an ERC starting grant in 2022.

Weaknesses and risks linked to the context

The need to respond to numerous calls for proposals, at a high frequency, in order to maintain high standard competitive research and stabilize research teams can be very restrictive and time consuming, and may slow down or even impede conceptual and technological advances, risk-taking and breakthroughs.

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

Strengths and possibilities linked to the context

Within the CIML, there are 6 platforms: Cytometry, ImagImm (imagery Immunology), Genomic, Bioinformatics, Histology and C elegans platforms. All these platforms are very well equipped with the latest technologies and personnel are dedicated to run them. These facilities are accessible to all teams of CIML. It is part of an attractive environment to welcome new teams leaded by young scientists (teams 2, 5, 8, 11 and 15,…) and the development of competitive projects. The genomic platform was implemented during the evaluated period. It allows to perform single cell RNA analysis and address new scientific questions.
Contracts with the various equipment companies are established to ensure maintenance of the devices and access to the latest innovations and core facilities managing committees decide on evolution of the platform with users. The CIML participate to instruments demonstrations with companies.
The platforms benefit from equipment grants from the Region SUD-PACA and team leaders are encouraged to finance new instruments on their grants (ERC). The Imaging Immunity – ImagImm – bioimaging core facility offers resources in advanced microscopy and is identified at the national level as "Infrastructure en Biologie Santé et Agronomie "(IBISA) and is part of the France BioImaging (FBI) network, a National Infrastructure in Biology and Health (INBS) laureate of the Program "Investissements d'Avenir" (PIA-ANR). All platforms have established quality protocols for their access and set-up and the ImagImm facility is under the quality policy ISO9001.
These facilities are fully financially supported by the CIML.

Weaknesses and risks linked to the context

Keep personnel dedicated to the platform (16 expert engineers or technicians run these platforms). The CIML hired 4 full time employees from Janvier Labs Company on its external funding sources. The single cell genomic core facility need the recruitment of a permanent engineer.
High cost to keep platforms up to date, renewal of obsolete key instruments.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

Outstanding productivity that needs to be continued with the arrival of very promising young scientists. They need to be supported at all levels to be able to keep up with this level.

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

Strengths and possibilities linked to the context

The emergence of innovative research themes relies on both the excellence of the science of the historical team at CIML as well as on the recruitment of young team leaders. The originality of the scientific production of CIML is justified by the extremely high-quality of the publications of the different teams in the last 5 years.
This is attested by the number of publications over the report period: 495 original research publications and 132 review articles, 80% of which were published in the most prestigious journals of their disciplines and 95% of which is available in open access. The quality of publications is outstanding with a large number published in top prestigious journals (*Nature, Nature Immunol, Cell, Cell Metabolism, Science, Science Immunol, Nature Comm, J Exp Med, PNAS) but also topic specific journals of excellent reputation (Immunity, Blood, JACI, Mucosal Immunol*). These notably include: 4 *Nat Rev Immunol*, 7 *Nature*, 10 *Science*, 12 *Cell*, 24 *Immunity*, 23 *Nat Immunol*, 19 *Nat Comm*, 24 *JEM*, …
The contribution to knowledge is evidenced by the impressive number of citations of CIML scientists over the report period, by the development of different patented methods (generation of different cell populations, metabolism profiling, single cell mRNA sequencing pipelines, …), algorithms and softwares, drugs (drug composition and engineered cells), and diagnosis methods or biomarkers. The new technologies are largely shared with other scientists at the National and International level, which has led to a substantial number of collaborative articles published in top-rank journals.

Weaknesses and risks linked to the context

No weakness.

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

Among the 18 group leaders at CIML, five are young investigators recruited from 2019 (teams 2, 5, 8, 11 and 15). A total of 670 publications are listed for all groups; over 400 of these published articles are original publications generated through the work of individual teams whereas 117 include several of the CIML teams; these numbers reflect high productivity by the unit and active intra-mural interactions. A variable number of articles has been published by the different teams varying between 3-87 articles; these variations are obviously related to the career stage of investigators but may also be affected by retirement plans.
All teams contribute to the publications' output and some of the teams appear to work in close connection with other CIML teams.
More than 300 publications have the members of the teams as first/last author and approximately 180 of these articles have CIML PhD students among authors.
The scientific production is proportionate to the research potential of the unit.

Weaknesses and risks linked to the context

There are not easily identifiable weaknesses in relation to standard 2 of scientific production.
It is however worth to reflect about the variable number of articles by the different teams and whether young investigators are provided with the best resources to succeed in their field of research, including mentoring programs and/or senior-young direct mentorship. There is no clear indication that general policies have been adopted at the unit level to synergize the efforts or guide the emerging teams.

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

Most teams put forward collegial decisions with respect to research directions, and collective discussions to ensure the theoretical soundness of the projects, the validity of the methodology, the solidity or irrefutability of the results. Solidity of the results is generally assured by independent repetition of the experiments, and use of proper statistical methodology. The soundness of theoretical and methodological foundations of the research developed at CIML is also empirically supported by the nature of the journals in which the results are published - many of the journals include internal "reporting summaries", "reproducibility checklists", and detailed method.

The unit has a well-defined data management plan and security of data storage and access, which is reinforced by the very active Bioinformatic team.

CIML has standardized lab-journals according to Inserm guidelines for all experiment and experimental procedures registration. All personnel performing experiments are required to have an up-to-date lab-journal. The center is currently implementing the electronic lab-journal Labguru, facilitated and approved by Inserm (https://cle.Inserm.fr/). The e-lab-journal, will be accessible to all team members according to their project. All entries will be documented and stored to enable traceability. Data storage will be allowed only on the dedicated and secured network-storage, which is backed-up regularly to ensure safety of the data.
Source codes are mainly used in the bio-informatics platform and supplied online on Github upon publication, as is requested by all scientific journals. Datasets on e.g. single cell sequencing are placed on NCBI Geodatasets after publication, in compliance with scientific publication rules.

All affiliations are mentioned correctly and all manuscripts are accessible through the national multidisciplinary scientific open archive database HAL (https://hal.archives-ouvertes.fr). The materials published are available to the scientific community, when necessary through an MTA, and the CIML frequently supplies mouse lines or other materials to groups outside the CIML. All data directly from the acquisition machines (raw data) is stored in a protected directory within the group directory. In case of complete cut to the outside, it is possible to access all data via the backup storage located within the local campus. Unused data is archived on tapes within the CIML and removed from the network storage. This data is always accessible to the researchers for retrieval.
The members of the team take part in scientific outreach activities, according to their scientific skills. They are present in the media, on internet or on social media, in compliance with research integrity and ethical requirements

Weaknesses and risks linked to the context

Unit's research activities and scientific production comply with scientific integrity principles and no specific weaknesses were identified. However, it is not clear whether there is a committee for scientific integrity in place, for solving any potential arising issues.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

Integration of CIML research activities in society is excellent. CIML teams have established solid and highly productive links with the socio-economic world and/or industrial partners. CIML team members actively participate to the dissemination of their scientific achievements to the general public and in providing scientific expertise to discussions with journalists.

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

Strengths and possibilities linked to the context

Two teams are part of the Institut Carnot "CALYM" a national consortium of research entities in the field of lymphoma. This Institute is committed to the development of research partnership with the socio-economic world. This includes launching calls, federating biobanks & platforms, organizing symposia, promoting joint research programs & valorization with the industry and national/regional valorization agencies (SATT-SE, Inserm-Transfert, CNRS innovation).
The Cancéropôle PACA supports several projects of the CIML. The CIML is one of the major partners of the Institute of Cancerology and Immunology (ICI), sponsored by the Aix-Marseille University and the AMidex Foundation. The ICI contributes to the integration of basic and clinical immuno-oncology research in the Marseille area with funding of students and post-docs.
CIML participates actively to other joint research programs, including the "Institut de Convergence CenTuri", that aims to understand of how biological function emerges from the organization and dynamics of living systems (https://centuri-livingsystems.org). CenTuri provides opportunities to perform multidisciplinary research with 20 institutes of the Marseille area. CIML also benefited from the support of the Aix-Marseille-University Idex (AMidex), receiving three Chairs of Excellence for new group leaders.
The CIML integration into the clinical environment, benefits from the Marseille-Immunopole cluster and immunoprofiling Platform (MI-PP) within the Hôpitaux de Marseille (AP-HM), that facilitates access to patient samples and clinical ressources. Through the MI cluster, CIML participate to the RHU "Pioneer Project" (https://marseille-immunopole.org/the-pioneer-project). CIML is one of the founders of MImAbs

(https://www.mimabs.org), an R&D Platform for the generation and characterization of immunotherapy antibodies.

Weaknesses and risks linked to the context

The CIML is located on the Luminy campus, close to other basic research institutes but it represents a barrier for the development of clinical research and maintain links with the different hospitals located within the Marseille area.

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

Strengths and possibilities linked to the context

The CIML has strong and long-lasting interactions with non-academic partners. Many teams of the CIML (12/19 teams) have partnerships with French or international pharmaceutical companies (Sanofi, Virbac, Beckman, Innate Pharma, Takeda, Medimmune, Alpine Immune, Bristol Myers Squibb BMS, Milteniy, Halio DX). Many projects of the CIML are supported by these companies (8 035 K€ during the evaluated period). These companies are attracted by the high level of researches of the CIML in different fields such as immunotherapy, vaccination, molecular typing of bacteria, neuro-imflammation diseases, tumor classification (WHO), 3D imaging of tumors, inflammatory bowel disease or the Lymphoma Single-Cell Atlas project. During the Covid19 pandemic, two teams oriented their research toward finding new therapeutic tools.
CIML was one of the founders of MImAbs (https://www.mimabs.org), an R&D Platform for the generation and characterization of immunotherapy antibodies. MImAbs was originally an industrial demonstrator financed by the PIA program and was transformed as an independent company in December 2020.
The CIMIL has contracts to provide continuing education to non-academic actors (imaging seminar series held at Sanofi),
At least one team hosted a person from a start-up company for 3 years.

Weaknesses and risks linked to the context

While CIML has started to foster interactions with non-academic institutions, it is still somehow lacking strong interactions with clinical partners.
Furthermore, while there is a decent amount of patents the question is if there is a clear roadmap to promote licensing and valorization of patents in terms of an ongoing tech-transfer management.
Despite the strong interactions with private companies, low number of PhD are funded by Cifre contracts (only one during the evaluated period).
There is a risk that collaborations and funding by private companies may lead to conflict of interest.
Except a great project mixing art and science, the unit has limited activities in citizen participatory science.

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

Strengths and possibilities linked to the context

Many of the unit's teams participated in an artwork exhibited at the Manifesta 13 International Biennial in Marseille and at the 36th International Digital Art Festival in Clermont-Ferrand. One team also participated in an art project at the Luma Foundation in Arles.
Most of the CIML teams participate in the science festival and some in days dedicated to their theme with patient associations.
As far as scientific mediation is concerned, this varies greatly from team to team. Access to the general public media seems to be easier for teams working on a topical subject related to a disease than for those doing fundamental research, but we can note the efforts made by all to popularize their subjects on the unit's website. And they all seem to be very willing to help when they are asked to do so, especially by schools.

Weaknesses and risks linked to the context

There is a great disparity between the teams, which could be detrimental to the public image of the CIML by highlighting only certain teams.

C – RECOMMENDATIONS TO THE UNIT

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

Hiring a dedicated person with relevant training, and/or integrating representatives of national or regional tech transfer offices (SATT, Inserm Transfert) might enhance the efficacy of the committee in charge of monitoring issues related to intellectual property and technology transfer.
The committee encourages the unit to continue its efforts to recognize the contributions of staff scientists and engineers/technicians in the teams through the CIML website and through organization of meetings providing transparency and promoting participation related to institute policy and development. The top-down communication can also be improved by circulating decisions of the unit's direction board through summary reports available on the CIML intranet.
The gender equality may be associated to actions such as discussion with personnel to identify new organization including equally male and female.
The unit should reinforce support for personal carrier development plans (notably, the yearly evaluation and promotion of engineers and technicians) of the permanent and non-permanent staff. The unit should also plan ahead and discuss in a top-down and anticipated manner with the ITA staff when teams are closing and engineers/technicians are to be redistributed to other teams. The new direction should favor dialog in order to prevent putting at stake the impressive cohesion of the unit in the future.

Recommendations regarding the Evaluation Area 2: Attractiveness

Very good scientists have joined CIML. They need to be supported and stay motivated to keep up with the outstanding productivity.
Concerning the collective well-being, a better recognition of non-team leader researchers and ITAs seems necessary. The establishment of working groups and a system for the review of ITA files by researchers other than the heads of staff eligible for promotion could help to create a feeling of transparency and equal treatment.

Recommendations regarding Evaluation Area 3: Scientific Production

Keep up with an excellent scientific productivity and pay attention to technological and workforce needs for new joining young teams.

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

Strengthen outreach activities towards the general public and/or patient organizations, by asking students to get involved in events for the general public, such as the science festival, my thesis in 180 seconds, etc…
Strengthen links with the industry.

TEAM-BY-TEAM ASSESSMENT

Team 1: From lymphoid structure to lymphocyte migration

Name of the supervisor: Mr Marc Bajenoff

THEMES OF THE TEAM

This team uses state-of the-art approaches such as lineage tracing, multicolor fluorescent reporter preclinical models and computational modelling to study the biology of stromal cells and their dialog with macrophages. Its research in the reporting period was structured along three axes. The first axis concerned the origin and behaviour in inflammatory as well as homeostatic conditions of lymph node stromal cells. In the second axis the team sought to characterize the hematopoietic origin of several immune cell populations. The third and most recent axis aimed to identify the stromal cell niches imprinting the identity of several specialized macrophage populations in lymph nodes and in the spleen.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The international visibility of the team can be increased by taking a more active role in the organization of topical meetings, conferences and symposia. We strongly recommend to take a more active role setting up collaborations with other (inter)national groups in the form of networks, consortia, or specific European actions.
Although the team has many interactions with other teams, an active role in networks or consortia was not developed.
It would be important to initiate interactions with hospitals and/or the industrial sector. The team is encouraged to also explore collaborations with non-academic partners. The committee of experts recommends to start dissemination activities to the general public.
Interactions with hospitals or industry, as well dissemination activities to the public have not been developed.
The committee of experts recommends that the team leader take gradually a more active role in decision-making committees including activities related to organization, scientific policies and research programs at the CIML, but also at the National level.
The team leader has not developed a more active role in decision-making committees at the local or national level.
The committee of experts recommends to take a more active role in the involvement in international and national training networks, in teaching and in the coordination of teaching activities at the master level.
A more active role of training networks or local teaching activities was not developed.

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	2
Non-permanent research supporting personnel (PAR)	0
Post-docs	2

PhD Students	0
Subtotal non-permanent personnel	**4**
Total	**5**

EVALUATION

Overall assessment of the team

This is an outstanding and exceptionally productive team with a single tenured scientist leader. He has developed an original research program focusing on stromal cell interaction with immune cell populations in lymphoid and non-lymphoid tissues, and acquired an internationally leading position in this field. The team has published a steady stream of top-quality publications involving most doctoral and post-doctoral trainees and is sought for as collaborator by many high-quality laboratories. The team faces a risk for its productivity due to the loss and non-replacement of two tenured staff.

Strengths and possibilities linked to the context

There are several reasons that render this team attractive. It has a leading position in the field of stromal cell crosstalk with immune cells, with the result that many other leading teams seek collaboration with it. The team collaborates with other top-level laboratories focusing on single-cell approaches to immune cells, macrophages in tissue environments such as liver, pancreas, bladder, testis, skin etc. This has provided access to preclinical models, expertise and high-dimensional omics approaches that allow the team to develop novel projects concerning different issue environments and physiological and pathological conditions and to apply state-of-the-art approaches of computational biology.
The team is also attractive for its technical expertise and opportunities. It has developed sophisticated preclinical models and has access to additional preclinical models that facilitate high-end mechanistic studies.
The team has a record of producing publications in top-ranked journals with doctoral or post-doctoral students as first authors, which will attract other young scientists to obtain training in it. Of the three PhD students and three postdocs, four obtained first author publications in top-ranked journals, one is finishing a project on pancreatic macrophages, and one decided to leave academia for an industry position.
The team has attracted significant funding mainly from national sources, five ongoing ANR projects fund different collaborations.
The team has made many original contributions in the three axes of research developed. In axis 1, this includes characterization of blood endothelial cell behaviour during lymph node inflammation and return to homeostasis, as well as trafficking of IgM through lymph node conduits in the early phase of an antibody response. Its studies in axis 2 have revealed that mast cells have dual hematopoietic origin, being derived from yolk sac precursors and hemogenic epithelium, while dendritic epidermal cells are derived from yolk sac precursors and replenished by self-renewal and expansion of tissue-resident "proliferative units". Recently the team focused on studies aiming to unravel stromal cell niches and scaffolds driving the tissue-specific differentiation of macrophages. In a series of three studies, the team could identify lymphatic endothelial cells as source of the mandatory growth factor CSF1 for lymph node subcapsular sinus macrophages, reveal that red pulp macrophages require WT1+ red pulp fibroblasts for differentiation and CSF1-dependent growth, and show that macrophages rather than previously suspected dendritic cells scavenge apoptotic cells in the T cell zones of lymph nodes.

Weaknesses and risks linked to the context

The team does not undertake efforts to develop "contributions to society".
The departure of two permanent members (one lecturer-scientist and one engineer) has resulted in significant loss of expertise in the laboratory and will necessarily slow down research even in the presence of satisfactory grant money, as expertise has to be newly acquired by incoming team members.

RECOMMENDATIONS TO THE TEAM

The committee recognizes that supervision by the team leader of all projects leaves little time for dissemination if the standard of excellence of the team's production is to be maintained. This notwithstanding, it encourages the team leader to develop limited engagement in dissemination activities, for example in teaching the scientific approach to problems to young students. Moreover, it encourages the team leader to consider opportunities for translational exploitation of the team's results in liaison with the relevant CIML committee, for example concerning targeting tissue-specific macrophage niches.

Team 2: Interferon Lambdas and Mucosal immunity

Name of the supervisor: Mr Achille Broggi

THEMES OF THE TEAM

The new team "INNATE IMMUNITY AT MUCOSAL SITES" (recruited in 2021) will explore the interplay between the immune systemand the mucosal epithelia with a focus on the role of the antiviral cytokine IFN-λ andits influences on Inflammatory Bowel Disease development.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Not applicable.

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

EVALUATION

Overall assessment of the team

The team fits very well in the overall strategic orientation of the CIML. Its work on Inflammatory Bowel Disease and the potential role of IFN-lambda is original and complementary to the other topics at the CIML. Hence, the team and its overall research vision has enormous upside potential in the CIML.

Strengths and possibilities linked to the context

The group leader has published in highly ranked journals in the past and he has an impressive track record.
In the first 6 months two pre-prints were submitted describing a novel role of IFN-λ in inhibiting epithelial regeneration in the gut and the description of two VEOIBD patients with deleterious mutations in IFN-λ.

Weaknesses and risks linked to the context

Not applicable; the team has recently joined the CIML and it is too early to judge on that.

RECOMMENDATIONS TO THE TEAM

Rapidly integrate as fast as possible; get involved in networking activities at the CIML and the whole Marseille research area (AMU et al).
The committee strongly encourages the team to be more involved in clinical research activities and networks to attract clinician staff and to get access to IBD patient samples.

Team 3: Dendritic cells and antiviral defense

Name of the supervisor: Mr Marc Dalod

THEMES OF THE TEAM

The team works to characterize the role of different types of Dendritic Cells (DCs), with focus on type conventional DCs and plasmacytoid DCs, in immune responses to viruses and tumors, integrating signaling by and interactions with innate immune cells e.g. NK cells. To do this it has established viral infection and tumor models, exploits its expertise in multicolor fluorescent microscopy and in bioinformatics applied to functional genomics, and develops preclinical models to track, gene-edit and delete DC populations. The team also developed a pipeline for in vitro genetic editing of human DCs.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The committee of experts recommends increasing the level of interaction with the social, economic and cultural environment. There are also patent possibilities that could be further explored, related either to methods of analysis developed by the team or to the transfer of knowledge on DCs derived from cord blood culture to guide translational/clinical research, for example in the context of immunotherapy.
One patent has been deposited during the period and the contribution to society seems little changed.
We encourage the two PhD supervisors to find the way to keep the quality of the PhD supervision while increasing the number of PhD students, if possible.
The team supervised 9 PhD students during the 5-year period.
Although the equilibrium between self-driven work and collaborative work was well monitored in the past period, it is a matter of concern for the next period. The committee of experts' recommendations are to take care of this point, to go deeper in the study on interactions between pDC and XCR1+ DC, as well as in the contribution of systems biology to integrating the results of different analyses at different scales. However the team requires funding to increase its expertise to develop this point.
The team has continued to study the interactions of both conventional and plasmacytoid dendritic with each other and with NK cells in the context of their activation and in models of anti-tumor and antiviral responses.

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	2
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)	1
Post-docs	2
PhD Students	0
Subtotal non-permanent personnel	**3**
Total	**7**

EVALUATION

Overall assessment of the team

Using complementary approaches and rigorous standards, this team has made original contributions to the understanding of the role of DCs in responses to tumors and viruses, published in high-quality journals. Use and development of original preclinical models for DC manipulation, multicolor fluorescent microscopy and functional genomics, and collaboration with first-rate groups have resulted in a production rated as excellent to outstanding. All students obtained publications though only half signing in the first position. The contributions of the team's activities to society are limited.

Strengths and possibilities linked to the context

Its broad and state-of-the-art expertise allows the team to obtain original results published in high-quality journals. As an example, the characterization of the modalities of pDC activation, published in papers in *Embo J* and *Nat. Immunol.* and signed by senior members of the team, used original reporter mice and single-cell RNA seq methods as complementary approaches.
Work published by the team established the critical role of Notch signaling for in vitro generation of human cDC1 from CD34+ hematopoietic stem cells. Linked to this work, the team has developed a pipeline for in vitro genetic editing of human DCs. The two papers mentioned above revealed several original aspects of pDC activation, including the (non-essential) role of Irf7, the requirement for physical interaction with infected cells, and the sequential nature of initial production of type I interferon followed by antigen presentation to T cells. The team also made important contributions concerning the crosstalk between NK cells and DCs in the initiation of anti-viral CD8+ T cell responses, and the role of several soluble mediators (XCL1, IL12, IL15, GM-CSF) in it.
The team published ten original articles, seven of them signed in (co-)dominant position by tenured team members. Four of these had excellent citation rates of >10 per year. Papers with dominant position were published in high-quality journals including *Nat. Immunol., Embo J.* and *Cell Reports*, and papers produced in collaborations in *Sci. Immunol., Immunity* and *J. Exp. Med.*
Among the five tenured scientists, four signed publications in dominant positions.
Among the 7 PhD students having defended their work or being about to do so, three have published original papers signed in the first position. On average, PhD students publish slightly less than one original article and 0.5 reviews. Among the five postdocs having worked for two years or more in the team, two left with first-author publications.
The team collaborates with partners of the highest international level, working for example at institutions in Belgium, Singapore, France and the US.
The team has obtained a one-year contract with the company KINATHERA concerning the role of interferon production by pDC in the treatment of respiratory infections. The team leader has consulted for the same company. Together with a researcher at the Institut Curie in Paris, the team has discussed with (non-identified) biotech companies with respect to exploiting pDCs and cDC1s in cancer immunotherapy, however these discussions have not yet resulted in a collaboration.

Weaknesses and risks linked to the context

The team has lost or is in the process of losing three tenured staff scientists. As the team leader is assuming the position of CIML director, the productivity of the team faces an important risk for the near future.
Although the team, with its five tenured scientist members, seemed until very recently in a position to develop non-academic interactions and products for the socio-economic world, and to share knowledge with the public, limited effort in this sense is recognizable.

RECOMMENDATIONS TO THE TEAM

The committee recognizes the risk for the team of the departure of multiple tenured scientists and encourages the team leader to identify scientists in terminating CIML teams or from outside CIML who could join the team. The committee encourages efforts to protect the unique and broad expertise of the team by reinforcing its staff, although thematic focusing, for example on research related to pDCs, may be required for a transitional period.

Team 4: Innate immunity in C. elegans

Name of the supervisor: Mr Jonathan Ewbank

THEMES OF THE TEAM

This team studies innate immune regulation in *C. elegans*. Using quantitative genome-wide RNAi screen and imaging / histology approaches, it analyses specific features of immune regulation including the link between wound repair and defense activation. The team addresses the dynamics and the pathogen determinants of regulation, and decipher how the virulence factors interfere with host signalling. The team also started to unravel how the extracellular matrix (ECM) modulates innate defenses.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The major recommendation of the previous Hcéres committee was to develop a translational research (for veterinary or human purposes) based the fundamental expertise and findings. The team leader discussed the fundamental focus of the research and the time from bench to «bedside». Importantly, he stressed out that the team research has longstanding impact, as revealed by duration of article citations.

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)	2
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	0
Subtotal non-permanent personnel	**2**
Total	**5**

EVALUATION

Overall assessment of the team

The Ewbank team has realized outstanding research using the innovative model of C. elegans, hypothesis-driven concepts and cutting-edge imaging, molecular and bioinformatics approaches. The recent discovery that mechano-sensing at membrane surface as well as the sensing of nucleolus integrity modulate innate immunity and wound repair highlights the originality and the impact of the team research and opens new prospects for mammalian biology.

Strengths and possibilities linked to the context

This team capitalized on a unique expertise on immunity in *C. elegans* and development of cutting-edge tools and bioinformatics. Thus, the team has an international recognition for this expertise and was able to continue ongoing collaborations and develop new ones. The team emphasizes a specific interest for the quality and the integrity of the data produced and published.
As described in the document, the team research is hypothesis-driven and curiosity-driven and this makes the research highly original and contributor to knowledge production.
The recent focus on ECM and immunity relationship and the virulence mechanisms of endoparasite of nematode are the main innovative development over the period. This research led to the production of articles in top-ranked journals with high visibility such as *PloS Genetics*, *Elife*, or *BMC biology*. The two principal investigators are both publishing as last and co-last authors, highlighting the leadership of studies. The team has also produced reviews in journals such as *Current Opinion in Immunology* or *Current Biology*. The team PI was appointed as editor in three journals and the principal investigators organized two international conferences and one MOOC.
The 4 PhD students having defended their work have published original papers signed in the first position. Among the four postdocs, two left with first-author publications.
The team has attracted significant funding, mainly from national sources, two ANR projects and one ANR-PIA project.

Weaknesses and risks linked to the context

The team now comprises few employees since the team leader is appointed since a few months to Inserm department dedicated to relations with EU. This unexpected change may be associated with the termination of activity of the team in the next years (after completion of ongoing funded projects).
A plan for reallocation of task force and resources in the next mandate is absolutely required.

RECOMMENDATIONS TO THE TEAM

The principal investigator that continue project leadership needs to prepare a contingency plan, thereby integrating the add-in value of the research activity for CIML and a fruitful and mutually beneficial reallocation of resources. Help from the unit's direction may be required to properly complete this process.

Team 5: B cells, Lymph nodes and Infection

Name of the supervisor: Mr Mauro Gaya

THEMES OF THE TEAM

The team develops a research project focused on the analysis of B cell responses during pathogenic situations. Using two models of lung viral infections, flu and SARS-CoV-2, the team has demonstrated the concomitant development of 2 populations of B lymphocytes (LB). One population of "bonafide LB" is specific for the cognate antigen(s) and produces high affinity antibodies. The second population of "bystander LB" does not produce specific antibodies but expresses high levels of Fc receptors; it thus retains immune complexes in the proximity of bonafide LB and reduces viral dissemination. The team exploits respiratory viral infection models and cutting-edge technologies (scRNA-seq, 3D imaging) to concomitantly study the B cell response to several antigens directly at the tissue barriers.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Not applicable due to the recent creation of the 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	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)	1
Subtotal permanent personnel in active employment	**2**
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	0
Post-docs	3
PhD Students	0
Subtotal non-permanent personnel	**3**
Total	**5**

EVALUATION

Overall assessment of the team

Young and promising team that has already made substantial contribution to the understanding of the polyclonal B cell response to different viruses. The team uses original preclinical models and exploit cutting-edge technologies with strong interactions with other Teams at CIML. Financial support has been secured with ERC and ANR grants for the coming years. The original work of the team and collaborative work have allowed 2 publications in high-quality journals. Engagement in communication and outreach and development of links with the non-academic socio-economical world remains limited.

Strengths and possibilities linked to the context

Team n°5 headed by Dr Mauro Gaya is a new team that joined the CIML in late 2019-early 2020. At the time of the report, the team included 1 CR, 1 research engineer, 3 post-docs and 2 PhD students.
The team studies the mechanisms regulating B cell responses to pathogens, particularly at mucosal surfaces. The research project is original and derived from novel observations from the team leader. The efforts since the creation of the team have led to 1 published high-quality article in Immunity (in which the team leader is the corresponding author), thus demonstrating a significant contribution of the group to basic scientific knowledge. Furthermore, M. Gaya has established collaborations with European scientists of the highest international level (Germany and UK). As an example, once such collaboration is dedicated to the characterization of unconventional T cells and lead to one high-quality article published Immunity in which Dr Gaya is a collaborator and that associates a PhD student of the team.
In the recent years, the team was supported by several funding grants including a Marie-Curie Reintegration fellowship, an early-career ATIP-AVENIR award (2020-2022), an Inserm Junior research award, and a European grant (LUNG BIM). The team has recently been granted by the ANR and an ERC starting grant.
The team is fairly young and it is too early to assess whether the "Scientific production is proportionate to the research potential". In the last 5 years, the team leader has published about 8 very high-quality original scientific articles, 3 of which were issued from the work of team n°5/CIML. Most of the task force of the team (2 of 3 Post-docs and 1 of 2 PhD students) have worked together to finalize the first original article published in Immunity. The other PhD student is associated with the collaborative article published in Immunity on non-conventional T cells. So far, none of the post-docs or PhD students have signed an article in first position yet, but a master student signed a publication in first position. The only research engineer attached to the team signs the article in Immunity as a first author.
The team is aware of the importance of communication and outreach, as shown by engagement in citizen participatory science activities through interactions with artists (example: Luma foundation in Arles), and by efforts to communicate in the Inserm journal. Because of its youth, the team is however putting emphasis on consolidating its national and international scientific recognition. First steps towards the development of links with the non-academic socio-economical world are nevertheless demonstrated by an ongoing collaboration with the non-academic partner Innate Pharma, and should grow in the future.

Weaknesses and risks linked to the context

This is a quite big team and all the post-docs and students have not signed articles as first authors as yet, which is important for their personal carrier development.

RECOMMENDATIONS TO THE TEAM

Ensure first author publication for all non-permanent staff.
The team is encouraged to exploit the originality of the research developed to foster intellectual protection and develop stronger links with socio-economic world.

Team 6: Immunology and cell biology of pathogen/host cell interactions

Name of the supervisor: Mr Jean-Pierre Gorvel

THEMES OF THE TEAM

This team studies the pathogenic bacteria *Brucella* and *Salmonella,* especially effector proteins secreted by type III and IV secretion apparatus. The main interest is to dissect the molecular mechanisms of effectors that subvert the immune system. The team is also involved in developing innovative prophylaxis approaches to improve vaccines and activation/expansion of tissue-resident memory T cells using pertussis toxin as an adjuvant for vaccination. More recently, a new topic was developed on malnutrition and its impact on microbial and immunological patterns using an innovative mouse model.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The overall quality of the body of knowledge was considered to not always match with high profile manuscripts, partly because the team was securing patents. During the last 5 years, the team has produced specialty profile publications in journals such as *Cellular Microbiology* or *Mucosal Immunology* but has, at the same time, continued valorisation.

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	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	**7**
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	2
Post-docs	0
PhD Students	0
Subtotal non-permanent personnel	**2**
Total	**9**

EVALUATION

Overall assessment of the team

The team is positioned in a unique field at CIML on bacterial pathogen – intestine interactions and develops research from fundamental aspects of pathogenicity and immunity to translational research on vaccines. During the evaluated period, the team had excellent tracking records, raised substantial funding from academic and private partnership and mentored a very high number of PhD students.

Strengths and possibilities linked to the context

The team has a unique expertise in CIML on host-pathogen interactions, especially oral bacterial pathogens and intestinal tract. The team has developed specific bacterial genetics to study the pathogenesis of Brucella and Salmonella at the cell and host level using innovative approaches of imaging and molecular analysis. The contribution of the team to the knowledge of interaction is also highlighted by the study of intestine-associated lymphoid tissue. Finally, the team strongly capitalized on the technical development and translation research on vaccines for valorisation (such as prototype development with companies). The team is also attractive for young scientists as shown by the integration of junior principal investigator and innovative projects such as malnutrition and microbe-immune interactions.
The team has a record of producing publications in top-ranked specialty journals with doctoral students as authors, such as *Cellular Microbiology, Mucosal Immunology, Journal of Cell Science, Cell Reports* or *Frontiers series*. Most principal investigators are both publishing as last and co-last authors, highlighting the leadership of their studies. The team has also produced reviews in journals such as *Nature Reviews in Microbiology*, *FEBS journal, or Mucosal Immunology*. Three principal investigators were appointed as editors in 12 journals and the team leader has leading position in two international societies (American Society for Microbiology and American Academy of Microbiology). Finally, the team declared one invention and delivered 3 patents during the period. The team (most principal investigators) obtained funding from national agencies (ANR x3, ANR PIA x1, Amidex x1, industry x1, tech transfer units x3, IRDx1, foundations x4).
Among the 13 PhD students, all who have defended their thesis, have published original papers signed in the first position or co-first author position. Most PhD students published also a review.
The team collaborates with partners of the highest international level (University Hospital RWTH Aachen Germany, Washington State University USA, Namur Research Institute for Life Sciences Belgium). The large number of collaborative articles support this activity.

Weaknesses and risks linked to the context

Two post-docs have only been hired during the period. This is rather low compared to the size and the resources of the team.
The activities of the team are spread over a rather broad spectrum.

RECOMMENDATIONS TO THE TEAM

Since the team will not be renewed as a CIML team, a contingency plan should be provided to figure out how the principal investigators of the team manage the organization of the activity, and the reallocation of task force and resources. Indeed, the team currently comprises a significant number of permanent employees (scientists and engineers/technicians). The team also has significant financial resources to continue activity over the 2024-2028 period.

Team 7: Membrane dynamics and lymphocyte signaling

Name of the supervisor: Mr Hai-Tao He & Mr Didier Marguet

THEMES OF THE TEAM

The research themes developed by this team are the biophysical principles governing the plasma-membrane lateral organization and the functional link between plasma-membrane dynamics and surface receptors. It thus works on the interface between physics and biology. Two groups operate within this team. The group led by Haï-Tao HE studies early, membrane-proximal events of T cell-signalling via the TCR, CD28 and cytokine-receptors. The biophotonics group of the team, led by Didier Marguet, develops algorithms and analytical tools for Single-molecule localization microscopy (SMLM), Fluorescence Correlation Spectroscopy (FCS), and Stimulated Emission Depletion Microscopy (STED).

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

"The team should continue in this research direction and further integrate knowledge within the fields of biophysics, photonics and immunology."
The team has continued and further developed its remarkable research on early events during TCR-signaling and integrated it with its activity on the biophysical and dynamic characteristics of the plasma-membrane.
"The international visibility of the team can be even further increased by continuing taking part in the organization of topical meetings, conferences and symposia."
The team co-organised two international forums on immunology, in Marseille-Luminy (2017) and in Shanghai (2018)
"The contribution to technology transfer and development of new microscopy modalities and software implementations is very highly valued and the team should further continue in this direction. It would be convenient to potentiate interactions with hospitals. Moreover, given the fact that the team develops new microscopy tools, they could also explore alliances with major microscopy companies."
The team participates to the EU H2020 FET OPEN project "LINKS" 2021-2025, a science-to-technology consortium which aims to develop, in collaboration with private companies, a lab-on-chip Terahertz biosensor combined with a fluorescence correlation spectroscopy module to investigate long-range electrodynamic interactions between biomolecules
In the framework of the "SATT SUD-EST – CONTRAT DE MATURATION PHASE 1" project "UNLOC − Imagerie microscopique de super résolution pour la biologie moléculaire", the team negotiates with French and German companies to license the commercial exploitation of the software package including MTT, UNLOC and QCM.
"The committee of experts recommends to involve more members of the team in scientific activities, including the generation of grants when possible, in addition to hands on research."
One of the staff scientists has obtained an ANR grant
"Increase the visibility (and participation) of PhD and Postdocs in the research being published by the group as the new generation will need to find stable positions in the future."
Among the 27 papers published by the team, 12 were published with team members as main author(s), and 10 with PhD student as author.
"The committee of experts highly recommends that other members of the team, aside from the PIs, also become involved in training and/or academic activities."
One of the staff scientists hold an associate professor position
"Attention should be paid to the recruitment of postdoctoral fellows."
Apparently, three postdocs were recruited into the team
"The committee of experts recommends to promote interactions with the medical sector in order to increase the impact and relevance of the research, and to increase collaborations with other members of CIML, for mutual benefits."
Three papers were published in collaboration with other CIML teams. Moreover, the biophotonics developments are transferred to the CIML common facility and thus made accessible to other CIML 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	2
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	0
Subtotal non-permanent personnel	**2**
Total	**9**

EVALUATION

Overall assessment of the team

This team works on long-standing and central questions in T cell-biology, developing and using state-of-the-art technology. It has an outstanding publication record and efficiently transfers its knowledge to the private sector. It was able to mobilize substantial funds for its research and has a very solid international visibility. Finally, it is actively involved in training of new generations of young scientists.

Strengths and possibilities linked to the context

The research themes of this team span the fields of biology and physics. This interdisciplinary approach has revealed substantial insight into early events of signalling in T lymphocytes. The team described that phosphorylation of PIP2 regulates binding of CD3e to the plasma membrane inner leaflet and thus its availability for interactions with kinases. Signalling through CD28 modulates TCR-induced calcium flux. The team also reported that the CD28/B7 affinity is regulated by signalling downstream of the TCR. It published that the glycosylation of the IFNgammaR2 guides it to sphingolipid/cholesterol nanodomains and is thus critical for activation of JAK/STAT signalling. Using the spot-variation fluorescent correlation spectroscopy (svFCS) methodology the team developed, it showed that one of the earliest events post TCR-engagement is a rapid and global transition of the plasma membrane dynamics. The latter induced an unbinding of the CD3e intracellular domain from the inner leaflet, allowing it to be phosphorylated. To study how serial triggering leads to T cell-activation, the team developed OptoFab, a light-controllable antibody Fab fragment capable of controlling TCR-activation. The team also further developed computational and experimental aspects of single molecule localization microscopy (SMLM), has optimized the sensitivity and extended the application of spot variation fluorescence correlation spectroscopy (svFCS), and has implemented a Stimulated Emission Depletion Microscopy (STED) imaging scanning microscope to complement SMLM-based studies and extend FCS applications. The intriguing results of this original research program were published in very good to outstanding journals (*Cell, Sci Reports, Sci bulletin, Frontiers in Immunology, Methods Cell Biol, Biophys J,* and *Methods*), a total of 27 papers, 12 as main author(s), 10 with PhD student as author, 3 in collaboration with another CIML team. Source code packages were made available to the scientific community. In collaboration, the team also contributed to the experimental detection of long-distance interactions between charged molecules by means of fluorescence correlation spectroscopy, a work published in *Physical Review E and Science Advances*. The scientific activity of the team was financially supported by five new contracts it obtained, four of which as PIs (2 ANR, SATT, FET-OPEN, M€1.2). The team negotiates with French and German companies to license the commercial exploitation of software packages. It participates to the EU H2020 FET OPEN project "LINKS" 2021-2025, a science-to-technology consortium which aims to develop, in collaboration with private companies, a lab-on-chip Terahertz biosensor combined with a fluorescence correlation spectroscopy module to investigate long-range electrodynamic interactions between biomolecules. The team filed a European patent protecting OptoFab and protects the algorithms it developed. Its members are regularly invited for talks in international meetings and have co-organised such meetings.

Weaknesses and risks linked to the context

Some existing administration measures from the institution bodies prevent post-docs and doctoral students not holding a permanent position and supported by Chinese grants to enter biology-laboratories and thus from joining the team, despite their success to obtain competitive fellowships. This hurdle in the recruitment of temporary staff is accompanied by the difficulty to find applicants with the required interdisciplinary expertise.

RECOMMENDATIONS TO THE TEAM

The committee encourages the team to continue the excellent work it has developed over the last years.

Team 8: Immune tolerance and T cell differentiation

Name of the supervisor: Mme Magali Irla

THEMES OF THE TEAM

The global theme of this newly established team (January 1st 2021) is the development of immune-tolerance in the thymus, with a particular focus on thymic stromal cells. Thus, during the reference-period, its team-leader and current members described that activation of RANK signalling improves regeneration of the thymus upon irradiation, that lymphotoxin controls entry of dendritic cells into the thymus and thus modulates induction of immune-tolerance and, in collaboration, that transforming growth factor beta promotes thymic deletion of autoreactive developing T cells.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Not applicable since this is a new team established in 2021.

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	0
Non-permanent research supporting personnel (PAR)	0
Post-docs	1
PhD Students	0
Subtotal non-permanent personnel	**1**
Total	**2**

EVALUATION

Overall assessment of the team

This team was created in 2021 upon a very competitive international call for new teams at the CIML. Since its creation, the young team has been very active in its field and has established a remarkable international visibility. The team has been very successful in obtaining research grants. It efficiently interacts with socio-economic partners and is strongly involved in training of new generations of scientists. The research activity of the young team has already yielded publications in excellent journals.

Strengths and possibilities linked to the context

This newly created team published five primary research papers in very good to excellent journals (*EMBO Mol. Med.* 2017, *Nat. Comm.* 2018, 2019, *eLife* 2022, *Cell Mol Life Sci.* 2022), four review articles (*Front. Immunol.* 2021a, 2021b, *Cell Death Differ.* 2021, *Annu. Rev. Immunol.* 2022), and several others in collaboration. Several of these publications were written during the Covid19-lockdown, illustrating a remarkable reactivity of the team. The team has produced five publications associating a PhD student in first name among which 3 scientific articles (*Embo Mol Med* 2017, *Nat Commun* 2018 and *Elife* 2022). Its fundamental research program has obvious links to potential important clinical applications (*e.g. Embo Mol Med* 2017): The team actively collaborates with Inserm Transfert and has filed three patents. This excellent scientific activity was financially supported by five research grants from *e.g.* the ANR, the ARC-foundation, and the "Agence de Biomédecine", totalling 550 k€. The team has acquired significant national and international recognition (e.g. an invitation to contribute a review article to the prestigious *Annu. Rev. Immunol.*, the Hélène Starck Award (ARC Foundation) for a PhD-student, a French National Academy of Medicine award for the team-leader). For the relatively small size of the team, it also has a strong involvement in teaching with six PhD-students and a postdoc (being) trained. The team-leader lectures at Master-level at the University of Grenoble.

Weaknesses and risks linked to the context

Currently the team hosts a single staff-scientist and it does not have a dedicated permanent technician.

RECOMMENDATIONS TO THE TEAM

Given the scientific success of the team, it should be able to attract other staff-scientists, which would further contribute to strengthening its structure. It will also be important to hire technical help, preferentially a permanent staff-technician. This team has made a remarkable start and should be encouraged and helped to continue in this way.

Team 9: Inflammation biology

Name of the supervisor: Mr Toby Lawrence

THEMES OF THE TEAM

Team 9 focuses on characterization of molecular pathways of macrophages and DCs, important cells in innate and adaptive immunity, in tissue homeostasis and immune-tolerance and their role in inflammation, autoimmunity and cancer.
Three themes are investigated to: 1) dissect the role of NF-kappaB pathway in dendritic cell maturation following their discovery on the role that Rank plays in maintenance of a subset of spleen marginal zone macrophages; 2) further characterize the role of NF-kappaB signaling in tumor progression based on the finding that IKKbeta deletion enhances melanoma immunogenicity; 3) elucidate the origin and function of tumor-associated macrophages; the group recently described different defined sub-populations of TAMs with immunosuppressive or trophic functions.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

On January 2018, 3 permanent researchers and 2 permanent staff were listed to be present in the team, previously indicated as team 7 under the direction of Lawrence Toby. Recommendations to the team in the previous evaluation campaign were focused on:
1) the need of developing further interactions with the social economic and cultural environment.
2) increasing the number of PhD students
3) comments related to the five-year plan in relation to experts to be involved in studies by the team on lipid metabolism remodeling to redirect macrophages' functions and cancer biology.

In relation to further interactions with the social economic and cultural environment: the PI is involved in the process of commercialization of research in collaboration with a start-up company. The team however does not work to provide documentation to social actors and does not participate in scientific outreach activities.
In relation to increasing the number of PhD students; two PhD students presented their PhD thesis during the reporting period and one additional student has been recruited in 2021.
The PI lists several international collaborators and these scientists work in the field of lipid metabolism and cancer biology.

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	0
Non-permanent research supporting personnel (PAR)	2
Post-docs	0
PhD Students	0
Subtotal non-permanent personnel	**2**

Total	**3**

EVALUATION

Overall assessment of the team

The scientific production is of excellent quality with publications in journals of high reputation obtained in two laboratories. The team has an excellent and relevant network of collaborators including some in the pharma industry. Important fundings were obtained.

Strengths and possibilities linked to the context

The team has published 31 highly cited articles in journals of excellent scientific reputation; members of the team were first/last author in more than half of these publications. The articles were published in collaboration with well-recognized international partners (including Imperial college London, King´s College London, Xinxiang Medical University, China) in the fields of immunology, tumor biology and lipid metabolism. There is a substantial participation of team members and PhD students to the publications. This is a significant achievement also considering that the team leader was spending a sabbatical period for a large part of the reporting period (2018-2022) at King´s College London. Both CIML and King´s College London are acknowledged in the publication.
One example of the high-quality publications is an article published in *J Exp Med* 2020 with the PI as last author where a specific role for tissue-resident macrophages was described in the context of invasive progression of metastatic ovarian cancer.
The team leader values capacity training of young investigators; two PhD students presented their thesis during the reporting period and 7 post-doctoral fellows worked in this unit; a large number of master students were also trained. An additional PhD student was recruited to the team in 2021.
The team attracted a large amount of research funds, mostly at the national level, including from ANR and INCa. Collaboration with important industrial partners was also established, including Sanofi and the PI received support from several industrial partners including Sanofi, Innate-Pharma and GSK; the PI participated in the GSK immunology network which is a platform for exchanges between academic teams and GSK.
It is relevant, also in the context of collaboration with non-academic partners, that the PI has produced three patents; one of these patents has been licensed by the start-up company OncoSpear ApS in which the PI participates as board member.
The PI participated in the evaluation of research grants for several granting agencies.

Weaknesses and risks linked to the context

In addition to his role as PI for the CIML team "biology and inflammation", the PI has a role as inventor and board member of a start-up company; he has also shown interest in management and administrative issues as he was previously appointed as CIML Deputy Director.
The team does not appear to participate in drafting of norms and procedures recognized by competent bodies, does not provide documentation to social actors and regrettably does not participate in scientific outreach activities.
Support from companies should be possible for PhD students training on programs at the interphase between academia and industry.
Clinical collaborations are not established in Marseille; this is remarkable as one of the motivations given for the period spent at King´s College London was the possibility of establishing collaborations with clinical centres.
Only two "Non-permanent research supporting personnel (PAR)" appear to work in the team.

RECOMMENDATIONS TO THE TEAM

The merits and reputation of the team are solid and should allow to attract funds at the international level; current grants available to the team are mostly supported by national agencies.
In view of the participation of the PI in the GSK collaborative platform it should be possible to recruit doctoral students financed by this non-academic partner to the CIML team.
Emphasis should be placed in consolidating the team through recruitment of post-docs and PhD students.
It should be possible to establish important clinical collaborations locally in Marseille.

Team 10: Genetic and structural analysis of T cell interactions

Name of the supervisor: Mr Bernard Malissen & Ms Marie Malissen

THEMES OF THE TEAM

This team dissects the function of T cells, dendritic cells and macrophages using a combination of non-supervised "omics" approaches and sophisticated genetic tools. It studies the functional heterogeneity of dendritic cells, the biology of skin macrophages, and signal-transduction in T lymphocytes. It thus described (in great detail) the surprisingly largely concordant differentiation of tolerogenic vs. immunogenic dendritic cells, the role of skin macrophages in tattoo persistence, the involvement of the RLT PR protein in signal transduction downstream of CD28, the proximal TCR signal transduction network, and provided a detailed view of several TCR-induced signalling pathways.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

No recommendations were formulated in the previous report besides continuing the outstanding work.

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	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	**4**
Non-permanent teacher-researchers, researchers and associates	2
Non-permanent research supporting personnel (PAR)	5
Post-docs	4
PhD Students	0
Subtotal non-permanent personnel	**11**
Total	**15**

EVALUATION

Overall assessment of the team

The research of the team, that is comprehensive characterization of immune cells by multiple techniques, is purely outstanding. Furthermore, there is an impressive and outstanding mentoring activity for the various team members.

Strengths and possibilities linked to the context

The team has an outstanding international visibility. It has an impressive publication record with 70 articles during the mandate of which 22 with a team-member as first, last, and/or corresponding author. These 22 articles were published in prestigious journals such as *Nature Immunology* (n=1), *Science Immunology* (n=2), *Immunity* (n=4), or the *Journal of Experimental Medicine* (n=3).
On 50% of the 22 publications, PhD students were authors. There are excellent and very productive collaborations within the CIML (12 out of the 70 publications). All tenured staff-scientists have published at least three first or last-author papers in the reference period and all doctoral students and all postdocs have published at least one first author paper in the reference period.
The team signed eight research collaboration contracts with industrial partners. The team has in general excellent activity in making the general the public aware of the team's research results (e.g. article in the *New York Times*, television interviews).
All the doctoral and post-doctoral students have obtained remarkable 'positions' at the end of their work in the academic and industrial world, refelcting the outstanding mentoring activity of the team leader.

Weaknesses and risks linked to the context

None identified.

RECOMMENDATIONS TO THE TEAM

The team leader will retire and the team will be suspended. Hence, there are no specific recommendations.

Team 11: Integrative B cell immunology

Name of the supervisor: Mr Pierre Milpied

THEMES OF THE TEAM

Using single-cell transcriptomic analysis, the team leader has shown that follicular lymphoma cells lose the synchronized gene expression patterns that characterize normal germinal center B cells. They uncovers the gene expression dynamics of human germinal center B cells, and their de-synchronization in germinal center-derived B cell lymphomas. They have developed and implemented integrative single-cell analysis methods and associated bioinformatics pipelines for the study of normal and malignant B and T cells. The team also developed a novel method that sequences the variable and constant regions mRNA frpm IGH and IGK/L, enabling the in silico reconstitution of complex BCR repertoires. The team now focuses on understanding the functional plasticity of B cells through 4 research axes: (axis 1) single-cell and spatial transcriptomics technology and data analysis, (axis 2) basic germinal center B cell biology in humans and preclinical models, (axis 3) functional plasticity of malignant lymphocytes in human lymphoma, and (axis 4) solid tumor-infiltrating B cells.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Not applicable since the team was created during the evaluated period.

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)	1
Subtotal permanent personnel in active employment	**2**
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	3
Post-docs	1
PhD Students	0
Subtotal non-permanent personnel	**4**
Total	**6**

EVALUATION

Overall assessment of the team

The team described the genetic divergence of malignant B cells in follicular lymphoma from their putative normal cell of origin. It has developed a unique study pipelines by combining expertise in immunology and single-cell data analysis, single-cell library preparation, bioinformatics data analysis, production of monoclonal antibodies and mathematical modelling. Financial support has been excellent.

The team has published several articles in very high-quality journals. Engagement in communication and outreach and development of links with the non-academic socio-economical world are limited.

Strengths and possibilities linked to the context

Team n°11 is a young team created in 2018 that originates from team 12. It includes a single permanent scientist and one permanent research engineer, and also includes 1 post-doc, 3 PhD students (1 student completed PhD during the evaluated period) and 3 non-permanent engineers. The team exploits its combined expertise in molecular biologists, cellular immunologists, bioinformatics data analysts, and mathematical modelling to train collaborators and develop the CIML Genomics core facility. This has fostered several collaborations over the years, both locally within the CIML and at the national level (CRTI, Nantes). The team has secured funding for a total 2 299 k€ between 2018 and 2025 (i.e., 287 k€/year). The grants originate from several national sources (PIA, ANR, Inserm, Cancéropôle PACA, INCA) as well as Associations or Foundations (ARC). The team also established a scientific collaboration with the private company Innate Pharma.
The team has published a decent number of publications in high and mid-impact journals 1 Nat Immunol (Milpied et al. 2018, first and co-corresponding author), 1 Immunity (Gregoire et al. 2022, co-corresponding author), 1 J Hepatol (Renand et al. 2020, co-last author), 1 Front Immunol (Attaf et al. 2020, last author), 1 Adv Immunol (Milpied et al. 2021, first author), 1 Eur J Immunol (Attaf et al. 2021, last author). High-quality publications have been published with teams at the CIML (2 *immunity*, 1 *Nat Immunol*, 2 *Cell Mol Immunol*, 1 *Sc Immunol*) or with French collaborators (1 *PNAS*, 1 *J Path*; 2 *iScience*, 1 *Plos Path*, 1 *EJI*). Two major papers of the team are in favourable revision in high-impact journals. A patent was filed on the FB5P-seq technology. The team has also opened the access to the codes, methods and pipelines of its bioinformatic tools, and has established databases (Depot NCBI GEO: GSE115795). The past PhD student has 4 original articles (2 as first author) and 1 review article (as first author). The 4 other PhD students and the only post-doc were recently recruited and do not have original articles as yet.
The team leader participated in a live interview in frame with Lymphom'Tour a communication event organized by a lymphoma patient association. He also involved himself in the scientific committee of Institut Carnot Calym and participated in the RHU "Pioneer Project". It also developed several interactions with non-academic actors, including a scientific exchange program with Innate Pharma, the involvement in the Institut Carnot CALYM consortium for research that fostered interactions with Institut Roche, and interactions with regular interactions with scientists from Bristol Myers Squibb to develop an ambitious Lymphoma Single-Cell Atlas project.
The team leader was elected as the deputy director for the next term with a very large majority of the votes of CIML employees. This should be an asset to re-motivate the scientific staff.

Weaknesses and risks linked to the context

All the collaborations listed in the report are established with French teams, and no international collaboration is highlighted. The number of interactions with the non-academic socio-economical world is very limited, as well as the development of products and involvement in outreach and communication activity. This may be explained by the youth of the Team which is probably still working on setting the basis towards its international scientific recognition.

RECOMMENDATIONS TO THE TEAM

Develop international collaborations.
Put in more efforts towards outreach and developing interactions with the industry.

Team 12: Genomic instability & human hemopathies

Name of the supervisor: Ms Sandrine Roulland & Mr Bertrand Nadel

THEMES OF THE TEAM

The team is at the forefront in deciphering the molecular events driving, from the early stages, the progressive transformation of B cells carrying BCL2 translocations into Follicular Lymphoma (FL). This is achieved through a balanced combination of genetic studies on B cells from healthy individuals and FL patients (reaching single cell resolution), and on genetically engineered preclinical models recapitulating major genetic lesions driving FL development. The team strength in studying lymphoid malignancies is further witnessed by genetic and functional investigations in the human and/or preclinical model setting, to unravel determinants influencing T-cell acute lymphoblastic leukemia onset, and B-cell acute lymphoblastic leukemia resistance to CD19 CAR-T treatment.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendation R1: Keep attention to in-house work and publications.
In the 2016-2021 period, team members appeared in 50 publications, including original research articles (33), review articles (11), book chapters (1), laboratory protocol articles (1), letters (1) and editorials (3). Team 12 members acted as first, last and/or corresponding author in 24% of all publications
R2: Increase connections with clinically orientated collaborators.
Team 12 has consolidated ties with local and national clinical centers. As member of the CALYM Carnot Institute, team 12 has the opportunity to analyze a growing number of clinically- and pathology-well annotated lymphoma specimens, also as part of open partnerships with pharma.
R3: Stronger involvement of senior researchers in the lab scientific organization.
Could not be evaluated
R4: The team should attract more PhD students.
Team 12 has slightly improved the the recruitment of PhD students from 4 to 6 units.
R5 Resources for lymphoma mouse modelling and human analyses should be balanced.
The teams keeps a good balance between the creation and analysis of improved FL preclinical models and an in depth analysis of human lymphoma specimens reaching single cell resolution.
R.6 Interaction with other national/international groups working in similar areas could help balance the risks.
Team 12 has built strong collaborations with leading laboratories studying lymphomas both pre-clinical models as well as human tumors.

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

Subtotal non-permanent personnel	**7**
Total	**13**

EVALUATION

Overall assessment of the team

Team 12 has carried out excellent research activities in the field of B- and T-cell lymphoma/leukemia pathogenesis. Strong translational drive inspired by top-notch molecular studies with growing attention to single-cell resolved analyses, improved pre-clinical tumor modelling and close link to industrial partners render Team 12 a reference laboratory for basic and translational studies in the field of lymphomas and leukemias.

Strengths and possibilities linked to the context

The team, internationally recognized for work on follicular lymphoma (FL), has gone in the last mandate through a major restructuring of its research program, investing on the development of more advanced and clinically relevant preclinical models, and on single-cell transcriptomics to deconvolute developmental trajectories of individual tumoral B cells of a large series of primary cases of FL, to ultimately capture the true essence of the malignant phenotype and its underlying molecular heterogeneity. This has led to a substantial potentiation of the bioinformatics framework sustaining the projects of the team, accompanied by the natural budding of team 11 with its leader, Dr Milpied coordinating the single cell technology platform running at CIML. In the evaluation period, the team has also led the bases for the conducting of large scale CRISPR/Cas9 genomics screening thanks to the productive stay of Dr Roulland in a laboratory abroad with advanced expertise in such technology At the same time, mouse and human projects centered on T-cell acute lymphoblastic leukemia and B-cell acute lymphoblastic leukemia have led to two publications in high-ranking specialist journals (*Nature Comm.* 2021, *Frontiers Immunol.* 2022). Overall, the team has produced a total of 50 publications, of which 8 original research article and 6 review/book chapters with team members acting as first/senior authors.
Dr Nadel received in 2020 the Prix Équipe à l'honneur by Fondation ARC and participated to flagship articles on human lymphoma biology, treatment and classification, including one for the World Health Organization. He is the Director of the Carnot CALYM Institute. Team members share responsibilities in learned societies (AICR, Société Française d'Immunologie, Société Française de BioInformatique), belong to editorial boards of high-rank specialist journals (*Frontiers in Immunology, Blood Cancer Discovery, Blood Advances*) and are regularly invited as speakers to top-notch national and international meetings.
Within the 2016-2021 mandate, the team has secured continuous funding (between 322 K and 1015K Euro/year) mostly from regional/national agencies (i.e., INCA, ANR, Cancéropôle PACA). Through the CALYM initiative, productive open partnerships with pharma (i.e. BMS, on the lymphoma single cell gene atlas program and for the generation of improved FL pre-clinical models) have ensured substantial financial support to the team (~2.6 million euros for the period 2019-2024).
The team has mentored 6 PhD students, 5 of which published at least one manuscript (4 as first author). Post-doctoral training was limited to 3 units.
The team has signed several R&D contracts with industry, including the CALYM/Celgene/BMS initiative.
The team is sensitive to the importance of communication and outreach, as witnessed by their engagement in several debates and dissemination to the lay public through media and conferences, of scientific contents and achievements of the team.

Weaknesses and risks linked to the context

During the last evaluation period, Team 12 has undergone a major reshaping of the scientific instruments supporting the research program in FL. Specifically, the team generated new preclinical models of FL and made substantial investments in bioinformatics, linked to the intensive use of single-cell transcriptomics and the estabslishment of a CRISPR/Cas9-based genetic screening program. Such reshaping of activities led to a transient reduction in the productivity of the group, with a limited number of original research articles published by the team members, acting as first and/or last/corresponding author, mostly on T-cell leukemia.
In the last mandate, post-doctoral fellow hiring was limited to three units (two of which in the past two years). Hence, despite the established international name recognition in the field of molecular hemato-oncology, and in particular FL, the team appears to have difficulties in attracting talented post-graduate experimental and clinical hematologists especially from abroad. Attractiveness towards bioinformaticians appears instead good.

Funding for several projects will expire in 2022 or get extinguished with the departure of Dr Payet-Bonnet, Funding from worldwide/European funding agencies and through international networking remains limited.

RECOMMENDATIONS TO THE TEAM

For the next mandate, attention should be placed to:
1) Increase the international visibility of the team, through organization of meetings, coordination of international networks in the context of Europe-funded training and funding schemes, and/or promoting international initiatives linked to the growing expertise of the team in single cell transcriptomics and/or large-scale cancer oriented CRISPR/Cas9 genomic screenings.
2) Improve attractiveness towards promising early-career international scientists including graduate students, post-doctoral fellows. The strong link with clinical centers should be pursued to recruit talented medical doctors at both national and international level who could further nurture the strong research program on lymphomas.
3) Equilibrate the current funding resources (currently based mostly on collaborations with industrial partners) with research grants from regional/national/international governmental/public funding agencies to protect the team from unpredictable changes in strategies imposed on the industrial partners by a rapidly evolving market.
4) Rapidly identify countermeasures to the departure of one scientist to ensure and further consolidate attractiveness, competitiveness and continuity in scientific productivity of the team.

Team 13: Tissue inflammation and immunity

Name of the supervisor: Mr Philippe Naquet

THEMES OF THE TEAM

The main research theme by team 13 is in unraveling links between metabolism and immunity. The team is specialized on tissue inflammation and repair during disease progression. This direction was undertaken by the team after their discovery, approximately two decades ago, of Vanin Pantetheinases thought to regulate coenzyme A-pathways. Genetic models were developed to study Vnn1 in gut inflammation and cancer. The work has a translational aspect and collaboration with clinicians working in the IBD and sarcoma has been established. Recent studies from the team provided novel information on the role that Vnn1 dependent generation of vitamin B5 has in limiting damage during tissue stress.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The recommendation from the previous report was addressed; this was mostly focused on poor interaction with other teams within the CIML. Clinical contacts (at Aix Marseille University, Pasteur Institute and others) and collaborations with scientists in the South remained prioritized by the team in the last reporting period.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	2
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	0
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	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	0
PhD Students	0
Subtotal non-permanent personnel	**0**
Total	**3**

EVALUATION

Overall assessment of the team

This team has pursued excellent scientific questions which are highly relevant to human diseases; the work addresses basic biochemistry mechanisms but has also a translational character.
The team has published important articles in journals of high scientific reputation.

Strengths and possibilities linked to the context

The research activities conducted by the team have scientific continuity since the discovery of the role of Vanin Pantetheinases in coenzyme A biology. The discovery gave the PI the opportunity to investigate the interface between inflammation and energetic metabolism in cancer.
The interdisciplinary approach between metabolism, inflammation and cancer is important and interesting.
The work by the team is well-cited; five original articles and 3 reviews were published by the team.
A recent work by the team published in the excellent journal Gut showed that enhancement of vitamin B5-driven metabolism by Vnn1induction during colitis can be a positive feed-back to mucosa healing; these findings can also have a therapeutic implication for improved anti-inflammatory therapy in IBDs.
Another important focus is on cancer biology; in the reporting period the team has studied Vnn1 role in various cancer models and in a recent work they showed that Vnn1, among regulators of mitochondrial activity, plays an important role in shaping the metabolic landscape in sarcoma (*J Hematol Oncol*). An ongoing follow-up study addresses the characterization of a mitochondrial molecule likely regulated by the product of Vnn1 enzymatic activity; in the cancer context this mechanism could reinforce CD8 and NK cells surveillance and cytolytic activity. This study will be completed in 2024.
The group has established clinical collaborations in France (Aix Marseille University, Institut Pasteur and other), in the USA (Pr Leonardi, West Virginia University) and South Africa (Erik Strauss, Stellenbosch University).
Due to age limit of the PI, this team will terminate its activity in 2024 and these last years of work will be devoted to study Vnn1 in Sarcoma.
One of the previous members of the team, Dr Irla Magali, has now become team leader at CIML; this is a positive sign of mentorship by the PI.
All tenured researchers in the team contribute to scientific production.
PhD training has been conducted by the team with a PhD who defended the thesis in 2018 and one who will present in 2023. These students were first authors in papers published in journals of good reputation.
Three patents were recently filed by the team; one is in the context of reparation of intestinal mucosa following inflammation.

Weaknesses and risks linked to the context

The team comprises very few employees; these appear however to be highly devoted to their work. The low number of employees is also motivated by the planned termination of activity of the team in the next 2 years.
The team does not have outreach activities which is due to time limitations; it would be important to inform different patient organizations on their important scientific work.

RECOMMENDATIONS TO THE TEAM

It is important to complete the important research projects before retirement of the PI.
Scientists in the team will join other CIML teams.

Team 14: Dendritic cell biology

Name of the supervisor: Mr Philippe Pierre

THEMES OF THE TEAM

Team n°14 studies several topics including the integrated stress response, autophagy and innate immunity receptor signaling. The research focuses on Dendritic Cell (DC) biology, with an emphasis on the importance of protein synthesis for antigen presentation and cytokines production, and of membrane traffic steps needed for DC functions. The team has shown the role of molecules from the integrated stress response pathway in immune and antiviral responses. It also identified BAD-LAMP/LAMP5 as unique marker for plasmacytoid DCs and molecular actors involved in the positive regulation of autophagy. The team develops innovative technologies, and has notably invented several puromycin incorporation-based technologies to monitor protein synthesis and energy metabolism at the single-cell level.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Team should continue participating in research networks and international collaborations on cell biology of dendritic cells...
Research networks have now been developed with EMBL, Portugal and Shanghai

No success in obtaining major network funding
Funding secured until 2025

The committee encourages continuation of dialog with public...
Outreach activities now include participation with "Nuit Européenne des chercheurs", participation in artistic events, communication in general press, radio shows, posting podcasts and raising awareness for kids.

The committee recommends to keep dual leadership of research team, especially in light of the heavier administrative load due to directorship by one of the PIs. The second PI should make sure that this benefit is not too much diluted by prolonged stays in Aveiro.

Dual leadership was not clearly mentioned in the report.
The coPI ended his coordination with the CNRS International Associated Laboratory "MISTRA"

Continuation of training international investigators at doctoral and postdoctoral level recommended, to continue international collaborations... Students should graduate with first author paper and publications in journals with lower impact factors need to be considered.

International networking has been continued with the hosting of a UCSF Professor in 2016 and a PhD student from the USA in 2018, collaboration with the Shanghai Institute of Immunology and the obtention of an ECOS-Sud grant in 2021. In addition, all PhD students graduated with a first author article

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	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	**5**

Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	4
Post-docs	0
PhD Students	0
Subtotal non-permanent personnel	**4**
Total	**9**

EVALUATION

Overall assessment of the team

The team develops original research with strong potential for valorization. It demonstrates excellent implication in dissemination, communication and outreach, with an excellent publication record and development of innovative technologies. The research is supported by constant funding, mostly from academic origin. The team also shows a good dynamic with the recent recruitment of two researchers. The team leader and his colleagues show strong engagement on activities linked to the management of research and other non-academic initiatives.

Strengths and possibilities linked to the context

The permanent staff in Team n°14 includes 4 researchers (2 recently recruited) and 1 engineer, completed by 4 post-docs and PhD students, and 4 engineers on non-permanent contracts (about 12.5 ETP). The team has raised 4 623 k€ for the period covering 2012 to 2025, which represents about 26 k€/EPT/year. The budget originates mainly from regional or national calls (ANR, ANRS, INCA, Canceropôle) or associations/foundations (ARC, FRM) with a notable misfortune in raising European grants, and limited support from the industry.
The team displays an excellent publication record with about 40 original and review articles since 2016 (15 where team members as the last author) published in high quality journals including *PNAS, Sc Signal, Cell Metabol, Nat Comm, Embo J*, and international recognition as attested by a review in *Science*. The team has also strong international collaborations in the US, Asia and Europe that led to publications in *Nat Comm, Nat Immunol, EMBO J*. All PhD students who completed PhD have one article as a first author.
The team has developed innovative technologies (SunRISE, SCENITH) that represent a breakthrough in the field for the study of metabolism at the single-cell level. The team is very much involved in developing products for the academic and social-economic world as witnessed by participation to guidelines for the use and interpretation of assays for monitoring autophagy, development of repository of unique short open reading frames (MetamORF), filing of 4 patents since 2018 (one licensed to Merk-Millipore), and ongoing development of a novel start-up "GammaOmics".
Members of the team are involved in the management of science: direction of CIML and participation as expert member of the ANRS study section for the Team leader, members or chair of Hcéres evaluation committees. The involvement in dissemination, outreach and communication is shown by the organization of symposium (CIML-EMBL workshops in 2017 and 2019, international forum in Immunology in 2017, CIML-Shanghai immunology institute in 2021), by articles in the scientific press (*Journal du CNRS*) or in the general press and interviews on radio shows as well as posting of podcasts. Dialogue with the general public is promoted by involvement of team members in "Nuit Européenne des chercheurs", artistic events (2019 Créations artistiques théorisées - MANIFESTA 13 – Les Parallèles du Sud) and awareness-raising actions with school pupils.

Weaknesses and risks linked to the context

Most of the original articles issued by the team are signed by the team leader as a last author. The team was able to establish few funding contracts with the private industry over the evaluated period. The team also did not succeed in securing funding from the EU.

RECOMMENDATIONS TO THE TEAM

It is important for the younger permanent staff to gain in visibility by taking the lead on published original articles, as an asset for the future.

The team is encouraged to secure funding from the pharmaceutical industry and from the EU using the ERC program (the achievements and originality of the work developed in the Team largely support the possibility) and other network initiatives.

Team 15: Infection of Meninges and Macrophages

Name of the supervisor: Ms Réjane Rua

THEMES OF THE TEAM

The team was created in 2019 with the recruitment of Réjane Rua as Junior Group leader (CRCN CNRS). The team focuses its researches on the brain immune defense system and in particular on the dense network of immune cells at the brain borders. The team has shown that meningeal macrophages are not only crucial to block brain infection, but are also required for proper brain development. Study on meningeal immunity revealed that the meninges contain a broad variety of immune sentinels that can start and amplify neuroinflammation. They also discovered that these cells are altered upon aging and that this age-related deterioration can be accelerated after acute neuroinfection. This opens up a broad area of research, as they discovered new players in the field of neuroinfection and neuroinflammation. This new discovery is a breakthrough on the crucial role of the meninges.
The team is using cutting-edge technology such as spectral cytometry, single cell nuc-RNA seq and in situ histocytometry to decipher the molecular mechanisms allowing the meninges to inform, protect and nurture the brain.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

New team created in 2019, not applicable.

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)	1
Subtotal permanent personnel in active employment	**2**
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	**4**

EVALUATION

Overall assessment of the team

This new team develops original research with high potential for excellent valorization. The publication level is excellent and the team develops innovative technologies. The team is supported by several grants, including national and European academic funding.

Strengths and possibilities linked to the context

The team benefits from several grants obtained in 2019 by the recently recruited young leader (Junior ERC 1 913 k€, Chair of Excellency from AMidex 60 k€) and in 2020 (ATIP/AVENIR 15 K€), Fondation pour la recherche sur le cerveau 80 k€ that allowed the recruitment of temporary personnel (PAR) and post-doc (Marie Sklodowska-Curie 185 k€) and equipment (Spectral Fluorescence cell sorter)(PACA region 55 k€).
The scientific production of the team is original with international co-publication in high-ranking journals (*Nature Immunology, Nature Neuroscience*).

Weaknesses and risks linked to the context

Since there is only one permanent researcher, she has to carry all the valorization, management and fund search for the next period.

RECOMMENDATIONS TO THE TEAM

A tenured researchers or associate professor recruitment would consolidate the promising themes of the team. The Team is encouraged to search funding from non-academic origin (industry) and to initiate collaboration with clinicians to develop projects on public health issues.

Team 16: From stem cells to macrophages

Name of the supervisor: Mr Michael Sieweke

THEMES OF THE TEAM

During the evaluating period Dr. Sieweke's team was interested in the biology of tissue-resident macrophages, their ontogeny, identity and self-renewal capacity in different physiological niches such as testis and lung.
The team also studied how epigenetic memory linked to infection history can be integrated in HSC and drive innate immune functions associated to a trained immunity response.
The integration of Dr. Alexopoulou's group to Dr. Sieweke's team also allowed the deployment of a topic based on the role of TLR signaling pathway in autoimmune diseases and the involvement of dendritic cells and innate immunity responses in this context.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

In the evaluating period, the recommendations made in the previous report were taken into consideration in the most appropriate way possible as follow:
Dr. Sieweke's team has included the former laboratory of Dr. Alexopoulou in 2019. This association has allowed Dr.Alexopoulou to gain visibility, and increase her interaction with the colleagues of the CIML. Moreover, Dr. Alexopoulou has established a collaboration with clinicians in the framework of her research theme on TLR axis-mediated autoimmune disorders.
Furthermore, PhD supervisions allowed Dr. Sieweke's team to ensure that the students produced a successful publication record as testified by the publication of scientific and review articles associating PhD students and their supervisors.

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

EVALUATION

Overall assessment of the team

The team has demonstrated an outstanding and unique contribution in the field of hematopoietic stem cell biology and macrophages. This was reflected by outstanding publications, local and international networks, exceptional capacity to raise funds and develop connection with industrial partners in the frame of translational research.

Strengths and possibilities linked to the context

In line with its strong and recognized expertise and technological skills in the area of HSC biology and myeloid differentiation, the team contributed to very original and major conceptual breakthroughs in the field of hemato-immunology. The team provided a rationale for the coupling of self-renewal and differentiation functions of macrophages, deciphered their ontogeny and cellular identity in the tissue (*Science* 2016, *J Exp Med* 2017, *Nature Immunology* 2022), and interfaced the fundamental properties of HSC that have epigenetically integrated the history of an infection, with the innate immune response in a context of global immune education (*Cell Stem Cell* 2020).
The scientific production of the team appears in outstanding publications.
The team has produced 12 publications directly connected with the themes' group, among which the PI appears last author in 8 scientific articles and 2 editorials in *J Exp Med, Science, Embo J, Cellular Immunology, Cell Stem Cell* and *Nature Immunology*. The team produced 11 publications in collaboration among which 6 with partners of the highest international level (MDC Berlin, Weizmann Institute Israel, Stanford).
All the tenured researchers contribute to the scientific productions:
A tenure researcher was co-last and co-corresponding author in the *Cell Stem Cell article*, contributed to an editorial as 1st author (*Nat Immunol*) and is author in the recent publication in *Nat Immunol* (2022), and participated to 2 collaborative publications (*Science*, *Cell*).
The researcher that joined the team in 2016 published 2 scientific articles as last author (*Frontiers in Immunology* 2019 & 2021), 2 articles in collaboration (*Journal of Immunology* 2016 & *J Exp Med* 2017) and is penultimate author In the article in *Nat Immunol* (2022). An associate professor, contributed to 2 articles among which one as co-last author (*Embo J.* 2017).
4 doctoral students among 5 that have defended their thesis, and 3 post-doctoral fellows contributed to the scientific production of the team with at least one article in first author in very good or even remarkable journals.
The capacity of the team to finance its research activities through external competitive funding is remarkable. The team is holder of 1 ERC Advanced Grant (1,147 k€), 2 ANR (~750 k€), 1 ARC (400 k€), 1 ITMO CANCER (158 k€) and 2 ARTHRITIS contracts (50 k€) and partner in 2 ANR (~350 k€).
Two patents applications of the team led to a delivery.
The team has an important institutional outreach (organization of conferences, stays in foreign laboratories) and members were awarded at a very high level (Knight of the National Order of Merit, bronze medal of the CNRS).
A tenure researcher was recruited by Inserm in 2020 after a post-doctoral fellowship in the team allowing a very relevant preservation of the scientific continuity. The 3 tenure researchers constituting the living force on site thus appear as an unavoidable asset for CIML.

Weaknesses and risks linked to the context

In 2018, following the team leader's new position abroad, the governance's modalities of the team were not clearly underlined. Although there are 3 permanent researchers on site, there is only one post-doctoral fellow and no new thesis students since the five thesis defenses (in 2018, 2019, 2020 and 2021) revealing a transformation of the team.
The leadership thus represented an important issue and was discussed during the interview.

RECOMMENDATIONS TO THE TEAM

Not applicable since the team is not renewed, the 3 tenure researchers in CIML are in process of joining other teams.

Team 17: Innate lymphoid cells and Neuronal regulation of immunity

Name of the supervisor: Ms Sophie Ugolini & Mr Éric Vivier

THEMES OF THE TEAM

Team17 includes two groups working on two independent programs. The Ugolini group develops the neural regulation of immunity focusing on four aspects: 1) the crucial role of the hypothalamic-pituitary-adrenal axis in tolerizing innate immunity to microbial endotoxin exposure; 2) The impact of the β2-adrenergic signaling pathway on host response during infections; 3) The therapeutic potential of NK in resolving neuropathy; 4) The essential role of sensory neurons in pain and tissue repair. The Vivier group is interested in ILCs, encompassing their cellular and molecular characteristics in mouse and human, and their role in disease with a specific focus on cancer. This group has developped therapeutic mAbs for which efficacy is currently being evaluated in clinical-trials.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

In the previous evaluation, most of the recommendations made were supportive. It has been suggested to the team to continue: 1) *Mouse and human studies on the tuning of NK responses in the clinical setting, and on the mechanisms behind NK education/memory; 2) International collaborations on innate lymphocytes in mouse and man;* 3) *Productive training of national and international investigators in immunology*. The committee has recommended however the following guidance: 1) *In addition to the school children visits, open house activities for the general public should be considered; 2) Reorganizing into two independent research teams with independent funding and distinct research topics could be considered; 3) The 2 main projects of the team (communication of the nervous & immune system, and ILCs) lack synergy and might be splited into 2 separate teams to strengthen thematic breadth of the CIML as well as a more favorable gender balance.*
Regarding the 2 first points, the team members' have strengthened their interactions with the general public through interviews with journalists from the scientific and general press. The team has set up a collaboration with primary schools and provides introductions to immunology for the pupils. The team participates in the dissemination of knowledge in society and interacts with the socio-economic world. Regarding the last point, the PIs aim to obtain the partition of the team into 2 independent teams or the renewal of the unit in 2024

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	2
Lecturer and associate lecturer	3
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)	2
Subtotal permanent personnel in active employment	**11**
Non-permanent teacher-researchers, researchers and associates	1
Non-permanent research supporting personnel (PAR)	3
Post-docs	2
PhD Students	0
Subtotal non-permanent personnel	**6**
Total	**17**

EVALUATION

Overall assessment of the team

The team includes two groups with different scientific programs: one focusing on the nervous system and immunity interplay and the second focusing on innate immunity in cancer. The scientific production is outstanding and is published in very high profile journals. The team has an excellent international network and pharma-industry partnership, and plays a central role in translating basic research into medical applications.

Strengths and possibilities linked to the context

The team includes two groups with different scientific programs. One group led by Dr. Ugolini is interested in the nervous system and immunity interplay and the second group led by Dr. Vivier is interested in innate immunity with a focus on ILCs and their role in cancer. This group has a significant contribution to the description and understanding of ILC biology. Team 17 productivity is outstanding with158 publications in total, including 93 scientific publications and 53 reviews published in journals with renowned profiles (*J Exp. Med, Nature Immunology, Immunity, Cell, Nature Comm., Nature, Science, Science Immunology, Science Signalling, EBioMedicine*). The team has contributed up to the fourth of the total output of the unit. The team has several international collaborations (Australia, USA, China, Korea), with joined scientific publications in high profile journals. PIs of the team have a close partnership with pharma-industry (Innate Pharma), which allows them to translate the basic research discoveries into clinical applications. The ILC group is present at 2 locations: Ciml and Marseille public hospitals (AP-HM). This set up together with the close link with innate Pharma has led to the development of innovative first-in-class therapeutic monoclonal antibodies such as NK cell engagers and monalizumab, for which efficacy against various cancers is currently being evaluated in clinical trials. The PIs filed 5 patents which is an outstanding achievement, and managed to raise funding from national and European public and charity institutions.
The team managed to secure research funding from different funding bodies including ERC (x3, ended in 2016, 2021 and 2022), RHU (x1, will end in 2022), ANR (x4, ended in 2019 & 2020, and one will end in 2022), ARC (x1, ended), LIGUE (x3, ended), FRM (x2, will end in 2024) and others less substantial from Inserm (ended).
The group leaders had several awards and distinctions, such as Chevalier de la Légion d'Honneur, ureka prize for scientific research Finalist, Khwarizmi International Award, Médaille de bronze du CNRS and le Prix Spécial Inserm. The team has also organized international conferences and members have numerous editorial roles, which is of great importance to CIML visibility.
Since its creation, two senior researchers have joined the team: an expert in myeloid cell biology and developmental immunology who was initially recruited as a post-doc and then succeeded in the selective competition for researchers at Inserm, thus obtaining a permanent position in October 2017. Also, an expert in immunooncology who was previously at the Curie Institute in Paris, and joined the team in September 2019.
Team 17 scientific output (past 5 years) relies on the participation of 12 PhD students (6 have finished), 15 permanent and non-permanent researchers including postdocs. PhD students publish their work in high impact journals as 1st, 2nd and/or middle author positions. The presence of clinicians within the team and their regular interactions with researchers is a strength for translational research.
This is quite a large team that aims to obtain its partition into two independent senior teams at CIML for the renewal of the unit in 2024.

Weaknesses and risks linked to the context

The two groups within team 17 target important research programs covering neuro-endocrine immune regulation and innate immunity in cancer respectively. However, during this past 5-year research plan, they did not show any synergistic scientific achievement, but an excellent individual achievement. Out of the 93 scientific publications, only 8% include both group leaders' names.
Regarding the collaborative work within the unit, team 17 interactions with other teams is weak, and counts only 6% of joined scientific publications.
The proportion of PhD students authoring scientific papers is up to 15%, which could be improved. Fifty % amongst them finished during 2018-2021 period. More students should be attracted to fulfill the balance. It is not clear how scientists with HDR and remaining students will be split in 2024 if two teams are created.
There is a good balance within the team in terms of scientific staff including PhD students, researchers, clinicians and technicians and it reflects the overall scientific productivity which is outstanding. But when it gets to the proportion of the staff included in each group (Ugolini and Vivier), aiming to split into two teams given that this is the goal for the renewal of the unit in 2024, it is quite difficult to understand how the staff will be split between the two and whether there will be an equilibrium in order to maintain the excellent scientific output.

There is no visibility on funding beyond 2022, except for the Ugolini group who secured an FRM budget till 2024. However, the amount of this funding won't be sufficient to achieve the different aspects of the scientific program.

RECOMMENDATIONS TO THE TEAM

The two group leaders have separate projects within the team and the scientific productivity in each group is remarkable. There is a lack of synergy between the two groups and therefore it would be advantageous indeed to consider splitting them into two independent senior teams at CIML for the renewal of the unit in 2024.
It would be important to anticipate the potential imbalance in PhD students and scientists holding HDR in both teams following the split, as this point is not quite clear.
Also, it will be important to plan the translational research in the neuro-immunology team as currently there are no clinicians in the future team and this is crucial given the ambition of the leader to develop clinical research based on recent data.

Team 18: Development of the immune system

Name of the supervisor: Mr Serge Van de Pavert

THEMES OF THE TEAM

Mr Van de Pavert's team is interested in the processes that drive the lymphoid system development. The team studies the formation of lymph nodes and lymphatic vasculature and focuses on the ontogenesis of lymphoid tissue inducer (LTi) cells. The team is also working on neuro-immunology aspects exploring the development of macrophages and innate lymphoid cells (ILCs) and their role in immune response in the context of cerebral diseases.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

An important concern was the high-level resources required to implement the research plan using mice. During the evaluated period, the team has followed the recommendation by securing funding with an ANR-PRCI grant, and with INCa and ANR-PRC grants in collaboration with the CIML.
The team has recruited 2 post-docs.
The team has kept its lead on the aspect of lymphoid tissue inducer cells ontogenesis and innate immune cells attested by major publications in 2020 and 2022.
The team has reinforced participation in international networks.
The team has set up a collaboration with biotech partners to optimize protocols for whole-mount imaging of tumors using the light sheet microscope.

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	2
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	0
PhD Students	0
Subtotal non-permanent personnel	**0**
Total	**3**

EVALUATION

Overall assessment of the team

The team has demonstrated an excellent contribution to very original scientific themes such as lymph node development, ILCs ontogeny and the role of macrophages in central nervous system. This was translated by major publications, important international collaborations and fund raising.

Strengths and possibilities linked to the context

The team has expanded by the arrival of a CNRS researcher, 2 post-docs, a permanent engineer, a contractual agent, and 3 PhD students. This has led to the completion of a large-scale and highly original work, directly attributed to the input of the team, contributing to a major advance in the understanding of the embryonic development of lymph nodes and the role of lymphoid tissue inducer cells in the ontogeny of the lymphoid system (*Cell Reports* 2020). The team also identified an unconventional population of perivascular macrophages in the brain parenchyma following stroke induction (*Nat Commun* 2022).
The team set up the whole-embryo 3D imaging, contributed to the establishment of an atlas on lymph node and settled a pipeline for the analysis of single cell sequencing data.
During the evaluated period, the team had an excellent level of publication with a total of 9 original scientific articles, among which the team leader appears in last name on the *Cell Rep*, and *Nat Commun* articles. The team also published 3 reviews, including one in *Nature Immunology*. The team co-published in the framework of international collaborations with renowned partners (Yale University, Dev Cell 2021, Jena University Germany, Glia 2018 and *Nat Commun* 2022, San Raffaele Scientific Institute Italy, *Immunity* 2022). All members of the team are associated with the publications. Particularly, the 2 post-docs have published as main author (*Dev Cell* 2021) and 2nd author (*Cell Reports* 2020) and the engineer has published as 1st author (*Nat Commun* 2022). PhD students that have defended their thesis have published or have publications in progress in first name.
The team interacts with other CIML groups. The group leader has demonstrated financial autonomy backed by scientific influence, notably by being the recipient of an ANR Collaborative Research Project – International (ANR-PRCI) grant (325 k€).
The team benefits from an institutional and international recognition. The team leader is the deputy director of the CIML, he has obtained the HDR and has a significant editorial activity. Furthermore, the tenure researcher who has joined the group has been awarded of the bronze medal of the CNRS.

Weaknesses and risks linked to the context

The team has not yet formally secured funding for the next mandate.

RECOMMENDATIONS TO THE TEAM

The team is encouraged to continue its fundraising momentum in aim at securing funding beyond 2023 to allow the successful deployment of original and important projects that were presented during the interview.

Team 19: Computational Biology, Biostatistics & Modelling

Name of the supervisor: Mr Sébastien Jaeger

THEMES OF THE TEAM

This bioinformatics platform provides direct support to research teams for the analysis of their results, experimental design and data storage. The team members are also responsible for the management of the equipment, software and user training.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The platform had not been previously evaluated.

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

EVALUATION

Overall assessment of the team

The CB2M platform has done an outstanding job in setting up an efficient operating system over the last few years, with a diversification of its collaborations and the implementation of original tools in their field. They are at the center of the CIML, helping all teams of the unit.

Strengths and possibilities linked to the context

CB2M (Computational Biology, Biostatisyics and Modelling) is organized and functions according to an original mode but which seems to perfectly suit the needs of the CIML. Being composed of only 4 statutory engineers (two of whom have recently arrived), they have chosen to encourage the teams with which they collaborate

to recruit bioinformatics students, whom they train and host in their premises. This has allowed the creation of a real bioinformatics cell where everyone has the possibility to exchange and progress.
From a practical point of view, they have set up a rigorous system of data management with notably a standardization of nomenclatures, storage as well as analysis methods which allows a great reproducibility of the results.
The scientific production of CB2M is original because of the diversity of the projects in which they are involved. Most of them are obviously linked to single cell and GSEA type data analysis but CB2M has started to collaborate with laboratories outside the CIML, especially in theoretical physics with even a collaboration abroad. This multidisciplinarity allows an original approach of biological questions with the use of modeling tools generally not much used. It also allows to put in contact teams that are not used to work together.
They have also developed two software programs used by the scientific community.

Weaknesses and risks linked to the context

During the evaluation period, CB2M had no funds other than those allocated by the CIML or obtained on very specific projects.

RECOMMENDATIONS TO THE TEAM

The platform should continue to develop its own projects and should mentor its own students (engineers, M2...) and look for raising its own funding.

CONDUCT OF THE INTERVIEWS

Dates

Start: 1st December 2022 at 08:00

End: 2nd December 2022 at 19:30

Interview conducted: on-site

INTERVIEW SCHEDULE

Interview day 1: 1st of December 2022

8h00 – 8h10 **Hcéres committee welcome**
Room: Yersin

8h10 – 8h35 **Hcéres committee meeting**
Room: Yersin
Closed-door meeting

8h35 – 8h40 **Hcéres rules and procedures by J. Dutrieux**
Room: Amphitheatre R-0
Public session (all unit members)

8h40 – 9h40 **Administrative and scientific presentation of the unit's achievements and future by P. Pierre**
40min presentation
20min discussion
Room: Amphitheatre R-0
Public session (all unit members)

9h40 – 10h00 **Committee debriefing and coffee break**
Room: Yersin ou amphitheatre
Closed-door meeting

Teams audition #1 *Public session (15min presentation + 15min discussion)*			
Time	**Room**	**Team Number**	**Presentation by**
10h00 – 10h30	Amphitheatre	1	Marc Bajenoff
10h35 – 11h05	Amphitheatre	9	Toby Lawrence
11h10 – 11h40	Amphitheatre	3	Marc Dalod
11h45 – 12h15	Amphitheatre	4	Jonathan Ewbank
12h20 – 12h50	Amphitheatre	5	Mauro Gaya

12h50 – 13h50 **Lunch break and committee debriefing**
Location: Yersin

Teams audition #2 *Public session (15min presentation + 15min discussion)*			
Time	**Room**	**Team Number**	**Presentation by**
13h55 – 14h25	Amphitheatre	6	Jean-Pierre Gorvel
14h30 – 15h00	Amphitheatre	7	Hai-Tao He / Didier Marguet
15h05 – 15h35	Amphitheatre	8	Magali Irla
15h40 – 16h10	Amphitheatre	2	Achille Broggi
16h15 – 16h45	Amphitheatre	10	Bernard Malissen / Marie Malissen
16h50 – 17h20	Amphitheatre	11	Pierre Milpied

17h20 – 17h45 **Committee debriefing and coffee break**
Room: Yersin or Amphitheatre R-0
Closed-door meeting

17h45 – 18h15 **Meeting with institutions representatives**
Room: Amphitheatre R-0
Closed-door meeting

18h15 – 18h45 **Committee debriefing**
Room: Yersin ou Amphitheatre R-0
Closed-door meeting

18h45 **End of day 1 Interview**

Interview day 2: 2nd of December 2022

Teams audition #3 *Public session (15min presentation + 15min discussion)*			
Time	**Room**	**Team Number**	**Presentation by**
8h00 – 8h30	Amphitheatre	12	Bertrand Nadel / Sandrine Roulland
8h35 – 9h05	Amphitheatre	13	Philippe Naquet
9h10 – 9h40	Amphitheatre	14	Philippe Pierre
9h45 – 10h15	Amphitheatre	15	Rejane Rua
10h20 – 10h50	Amphitheatre	16	Michael Sieweke

10h55 – 11h15 **Committee debriefing and coffee break**
Room: Yersin or *Amphitheatre R-0*
Closed-door meeting

Teams audition #3 *Public session (15min presentation + 15min discussion)*			
Time	**Room**	**Team Number**	**Presentation by**
11h20 – 11h50	Amphitheatre	17	Sophie Ugolini / Eric Vivier
11h55 – 12h25	Amphitheatre	17bis	Sophie Ugolini / Eric Vivier
12h30 – 13h00	Amphitheatre	18	Serge Van De Pavert
13h05 – 13h35	Amphitheatre	19	Sébastien Jaeger

13h35 – 14h15 **Lunch break and committee debriefing**
Location: Yersin

Meeting with unit staff *(In the absence of managing staff)*			
Time	**Room**	**Committee Number**	**Meeting**
14h20 – 15h00	TBD	1	Meeting with ITAs (*in French*) - 77
	TBD	2	Meeting with researchers - 52
	TBD	3	Meeting with PhD students and postdoctoral fellow - 69

15h00 – 15h25 **Committee debriefing and coffee break**
Room:
Closed-door meeting

15h30 – 16h10 **Meeting with the unit direction**
Room:
Closed-door meeting

16h15 – 18h45 **Redaction of the final report**
Room:
Closed-door meeting

18h45 **End of the interview**

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-PUR230023034 - CIML - Centre d'immunologie de Marseille-Luminy

Marseille, le mardi 18 avril 2023

Madame, Monsieur,

Je fais suite au mail que vous nous avez adressé le 07/02/2023 dans lequel vous me communiquiez le rapport d'évaluation Hcéres de l'Unité CIML - Centre d'immunologie de Marseille-Luminy.

Comme demandé dans ledit mail, je vous fais part des observations de portée générale remontées par l'unité et les tutelles n'ont pas d'autres commentaires.

En tant que directeur du CIML, je remercie le comité d'évaluation HCERES pour l'étendue de son travail, la qualité de son rapport et l'appréciation « outstanding » pour l'évaluation globale des performances du CIML pendant les 5 dernières années. Bien que très fier de cette évaluation, je dois faire quelques observations sur quelques points soulevés dans ce rapport concernant l'unité. Vous trouverez mes commentaires à la suite des remarques et recommandations globales issues du rapport, suivis de points précis soulevés par certaines équipes du centre.

GLOBAL ASSESSMENT

The global performance of the CIML unit is outstanding. p6

We are very proud that the HCERES committee has judged the scientific accomplishments of CIML to such a high degree, and we hope that CIML governing bodies will ensure a continuous support to the Institute to maintain the excellence of the research performed in the coming years.

To what extent the reshuffling of many teams will impact on the careers of permanent researchers, graduate students, engineers and technicians involved in these movements is presently difficult to estimate, and represents an aspect of the future unit's life. The new scientific direction will need to assess this with great care. In support of this, a higher transparency of decision making processes and improvement of top-down communication to the personnel (researchers, engineers, and technicians) is encouraged. Closer mentoring by the scientific direction and team leaders, of permanent staff (researchers, engineers, technicians) for timely planning of suitable career paths, together with offering a stronger visibility to, and care for lab personnel needs is expected to improve the Unit's spirit. Revising and optimizing the administrative support for non-French-speaking researchers will help to further increase the excellent international visibility CIML has, contributing to attract more foreign researchers. p6

All these points have been identified prior to the committee's visit, and the past and future management teams (2024-2028) have prioritized their actions to solve these issues. Higher transparency of decision-making processes and improved communications with the personnel have been implemented. These actions will be reinforced by the new direction team.

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

CIML scientists globally have access to outstanding resources. This includes free in-house and additional outside core facilities, excellent third-party funding, efficient interaction with medical institutions providing opportunities for translational research and with private companies, and implication in several undergraduate programs attracting students to CIML.

However, CIML faces a risk to the level of excellence of its functioning and specifically core facilities, due to rising costs, only partly appropriate calls for equipment replacement and partial replacement of departing staff. p7

We thank the committee for its evaluation and fully agree with the last statement underlining the need for adapted equipment calls and departing staff replacement by the governing bodies of CIML.

The scientific objectives of the unit are excellent. p8

The research center is very well organized. It includes outstanding State of the Art Technology Platform. p8

We thank the committee for its praising evaluation

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

CIML receives about 28% of the yearly budget of about 5.4 M€ from its supervisory authorities. CIML has adopted the relatively uncommon model of supporting with this budget not only common expenses, infrastructure and administrative services, but also to make access and use of its seven core facilities and its two animal facilities free of charge. P8

It is important to underline that this 5.4 M€ yearly budget does not include the salaries of staff researchers and engineers provided by CIML governing bodies.

It is also important to indicate that access to the core facilities is not "free of charge", it is costly! The burden of these expenses is partially taken care by CIML community, through the core budget (dotation) and for the animal facilities, also both by specific team externals grants and available overheads, which are used to support the hiring of external animal caretakers.

Weaknesses and risks linked to the context

Although CIML has set up a committee monitoring (next to international relations) issues related to intellectual property and technology transfer, it is unclear whether researchers have all the competence required for identifying and managing these issues on their own.

CIML researchers do not have all the competences required to manage IP issues. This is why CIML benefits from the expert support of its different governing bodies IP support subsidies, including Inserm Transfert, SAAT Sud-Est, CNRS Innovation, ProtisValor, that help on a daily basis CIML researchers to transfer and protect the valuable results of their innovative research. We have here to underline the strong and dedicated role of Inserm Transfert to support CIML researchers in all valorization activities, a point that might not have been stressed enough during the evaluation.

At the societal level, several Teams are involved into the translation of their research into clinical development (mainly early clinical trials). In the evaluation period there was 1 biotech created and 24 patents filled, which is excellent. p9

Funds from Inserm-Transfert (175 k€) and the Société d'Accélération de Transfert de Technologies (SATT) (>770 k€) also contributed to the economic vitality of the research structure. p12

These statements provided by the committee itself further supports the important role of IP transfert and patent offices to promote the patenting and translational process at CIML.

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

Weaknesses and risks linked to the context. p9

While CIML has started to foster interactions with non-academic institutions, it is still somehow lacking strong interactions with clinical partners. Furthermore, networking activities are mainly driven by few well established team leaders and there seems to be no overall strategy of the unit's direction to establish a CIML headed immunological research hub at the local or national level, as it might be appropriate for the leading French institute in all areas of immunology.

As underlined by the report, CIML is well integrated in its environment, notably through the creation and participation to Marseille Immunopole and AMU Institut Cancer et Immunologie, which are themselves local Immunology hubs to support clinical and industrial transfer. The CIML has therefore already developed a strategy for interacting with clinical and industrial regional partners. Moreover, a plan for developing a clinical core facility of CIML at the Timone Hospital has been proposed to the governing bodies for the future, however this was not included in the evaluation report given the prospective nature of this request.

It is unclear how the engagement into the Carnot Institute is supposed to contribute to the institute's revenues. Furthermore, while there is a decent amount of patents, the question is if there is a clear roadmap to promote licensing and valorization of patents in terms of an ongoing tech-transfer management. p9/p10

In the current 2020-2024 Carnot mandate, 2 CIML Teams are member of and benefit from the Carnot label. The Carnot CALYM Institute provides to its members a professionalized environment to boost partnership with the industry and the means to progress in the TRL scale of a project, from discovery to translational to clinics. Through CALYM's sourcing and project management activities, several ambitious industrial partnerships (>4M€) have been signed in the last period with the CIML teams, and several prospects are currently in progress. Besides direct revenues, CALYM membership also opens access to a structured consortium, including state-of-the-art platforms (e.g., the French Connect ctDNA platform), sample collections and databases (e.g., the Lymphoma Data Hub for AI), all of which represent attractive assets for industrial partners. In the next Carnot application (2025-2028), the Carnot CALYM Institute will be structurally engaged in the Carnot/MESR plan to double global Carnot revenues (from 500M€ to 1Md€ by 2030), through several growth drivers, among which the conversion of agnostic academic labs to industrial partnerships. The CALYM's "open innovation" model (shared risks of upstream research and shared ownership of discoveries) is particularly attractive to fund upstream research while getting the professionalized support to transform discovery into therapeutic innovations, all the way to market access.

According to the Carnot/MESR plan, the CALYM Carnot Institute and CIML plan for the next Carnot mandate to enlarge the CIML label perimeter from 2 CIML teams to the whole CIML UMR. In this context, all CIML investigators involved in innovations linked to lymphoid neoplasia (including development of immunotherapy), will be eligible to CALYM's accompaniment and industrial network to build recurrent industrial partnership. Considering the impressive innovation potential of CIML teams, one might expect at a very minimum to double the revenues of the current period (objective ~10M€ by 2028), while entering into the virtuous circle of industrial collaboration through professionalization and long-term renewed partnerships (as is the case for actual Teams with the BMS Biopharma).

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

Weaknesses and risks linked to the context. p10

The number of "assistant de prevention" is relatively low with regard to the number of personnel, especially the short- mid-term contracts that constitute 50% of the human resources.

CIML has now 3 assistants de prevention. This number increased during the time gap between the report filing and the site evaluation, and seems not to have been considered in the committee report.

Interviews with the non-leading scientific staff and with the technical/engineering staffs independently pointed out some degree of frustration in terms of recognition. The technical staff expressed lack of, or minimal, support from some team leaders and/or from the direction for their personal carrier development plans.

This is an ongoing problem, which is partly due to the global organization of the French research system, the management of CIML is well aware of this issue and it will be a priority of the next direction team to improve this situation.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit. p10

The attractiveness of the unit is excellent. The members of the unit are strongly recognized for their major scientific contributions in the fields of fundamental and applied immunology, and cancer biology. CIML is a very attractive structure for students and post-docs interested in advanced training in immunology and for young researchers who wish to pursue their own research programs. Outstanding fund raising capacity, with state-of-the-art technological platforms greatly contribute to CIML attractiveness.

We thank the committee for these praising comments.

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

Weaknesses and risks linked to the context. p11

No weakness identified.

We thank the committee for these praising comments.

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

Weaknesses and risks linked to the context. P11

Half of the ITAs are non-statutory and this is a weak point in the lab's memory. After discussion with the different categories of staff, there seems to be a feeling of lack of recognition in some teams.

We are completely in line with these comments, for the first part, we depend on the strong and recurrent support of our governing bodies to secure permanent ITA positions and ensure the replacement of departing ones. For the second point, this issue concerning few individuals has been identified, and improving their situation is part of the objectives of the next direction team.

3/ The unit is attractive because of the recognition gained through its success in competitive calls for projects. P11

Weaknesses and risks linked to the context. p12

The need to respond to numerous calls for proposals, at a high frequency, in order to maintain high standard competitive research and stabilize research teams can be very restrictive and time consuming, and may slow down or even impede conceptual and technological advances, risk-taking and breakthroughs.

We fully agree with this comment, this issue is a general problem in the French research system, as documented by a recent report of the Cours des Comptes.

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

Weaknesses and risks linked to the context. p12

Keep personnel dedicated to the platform (16 expert engineers or technicians run these platforms). The CIML hired 3 full time employees from Janvier Labs Company on its external funding sources. The single cell genomic core facility need the recruitment of a permanent engineer. High cost to keep platforms up to date, renewal of obsolete key instruments. P12

We hire 4 full time employees from Janvier Labs Company. We hope that CIML governing bodies will improve their support to maintain the excellence of the research performed at CIML in the coming years and provide much needed positions of permanent engineers and financial renewal plans for obsolete equipment.

EVALUATION AREA 3 : SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

Outstanding productivity that needs to be continued with the arrival of very promising young scientists. They need to be supported at all levels to be able to keep up with this level.

We thank the committee for these praising comments.

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

The originality of the scientific production of CIML is justified by the extremely high-quality of the publications of the different teams in the last 5 years.

Weaknesses and risks linked to the context. p13

No weakness.

We thank the committee for these laudatory comments.

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

There are not easily identifiable weaknesses in relation to standard 2 of scientific production. p13

We thank the committee for these laudatory comments.

It is however worth to reflect about the variable number of articles by the different teams and whether young investigators are provided with the best resources to succeed in their field of research, including mentoring programs and/or senior-young direct mentorship. There is no clear indication that general policies have been adopted at the unit level to synergize the efforts or guide the emerging teams. p13

It has been a policy of the CIML direction to provide extensive support to young teams, which benefited from permanent ITA support and constant help from CIML to establish their laboratories and apply to young investigator programs. They also benefited from both the mentoring by a senior colleague from CIML and a mentor from a different institute nominated by CNRS or Inserm. CIML has also made mandatory for new group leaders to follow international laboratory management courses.

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

Weaknesses and risks linked to the context. p14

Unit's research activities and scientific production comply with scientific integrity principles and no specific weaknesses were identified. However, it is not clear whether there is a committee for scientific integrity in place, for solving any potential arising issues.

We thank the reviewers for these laudatory comments. In addition to the rules of good practice of research implemented in all the teams, CIML fully relies on national scientific integrity committees from CNRS or Inserm to solve any potential arising issues, that could be treated in full independence and transparency if required.

EVALUATION AREA 4: CONTRIBUTION

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

Integration of CIML research activities in society is excellent. CIML teams have established solid and highly productive links with the socio-economic world and/or industrial partners. CIML team members actively participate to the dissemination of their scientific achievements to the general public and in providing scientific expertise to discussions.

We thank the committee for these praising comments.

Weaknesses and risks linked to the context. p15.

The CIML is located on the Luminy campus, close to other basic research institutes but it represents a barrier for the development of clinical research and maintain links with the different hospitals located within the Marseille area.

A plan for developing a clinical core facility of CIML at the Timone Hospital has been proposed to the governing bodies for the future, however this was not included in the evaluation report given the prospective nature of this request.

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

Weaknesses and risks linked to the context. p15

While CIML has started to foster interactions with non-academic institutions, it is still somehow lacking strong interactions with clinical partners. Furthermore, while there is a decent amount of patents the question is if there is a clear roadmap to promote licensing and valorization of patents in terms of an ongoing tech-transfer management.

Again CIML benefits from the support of IP transfer and valorization subsidiaries that are in charge of the licensing and valorization of patents.

Despite the strong interactions with private companies, low number of PhD are funded by Cifre contracts (only one during the evaluated period). There is a risk that collaborations and funding by private companies may lead to conflict of interest. Except a great project mixing art and science, the unit has limited activities in citizen participatory

The CIFRE Program is somehow impaired by the complexity of IP sharing among the two partners given that most candidate program starts from pre-patented discovery by the industrial partner, which is not eligible to a CIFRE partnership with academic laboratories. Importantly, all activities and contracts of CIML permanent and non- permanent researchers are framed by the employers and the different academic research valorization laws, leaving little space for conflict of interest with private companies activity.

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

Weaknesses and risks linked to the context. p16

There is a great disparity between the teams, which could be detrimental to the public image of the CIML by highlighting only certain teams.

We are not certain of what could be detrimental in the highlighting of certain teams for CIML image, given the "esprit de corps" of the Institute and the great care with which CIML controls its external communication and the visibility of its scientific or social activities. However, the non-replacement of a permanent communication officer by the governing bodies has seriously altered the external communication capacity and its outreach to the society during the last mandate.

C – RECOMMENDATIONS TO THE UNIT

Recommendations regarding the Evaluation Area 1: Profile, Resources and Organization of the Unit. p16

Hiring a dedicated person with relevant training, and/or integrating representatives of national or regional tech transfer offices (SATT, Inserm Transfert) might enhance the efficacy of the committee in charge of monitoring issues related to intellectual property and technology transfer.

This recommendation does not take in account the key role of the different IP transfer and valorization subsidiaries of the governing bodies and the activity of Dr. Sophie de Benzmann at CIML (DR Inserm), who's function is to facilitate the interactions of CIML with the industrial world.

The committee encourages the unit to continue its efforts to recognize the contributions of staff scientists and engineers/technicians in the teams through the CIML website and through organization of meetings providing transparency and promoting participation related to institute policy and development. The top-down communication can also be improved by circulating decisions of the unit's direction board through summary reports available on the CIML intranet.

The gender equality may be associated to actions such as discussion with personnel to identify new organization including equally male and female.

The unit should reinforce support for personal carrier development plans (notably, the yearly evaluation and promotion of engineers and technicians) of the permanent and non-permanent staff. The unit should also plan ahead and discuss in a top-down and anticipated manner with the ITA staff when teams are closing and engineers/technicians are to be redistributed to other teams. The new direction should favor dialog in order to prevent putting at stake the impressive cohesion of the unit in the future.

These suggestions are currently being implemented since January 2022 and will be developed in the next mandate.

Recommendations regarding the Evaluation Area 2: Attractiveness. p16

Very good scientists have joined CIML. They need to be supported and stay motivated to keep up with the outstanding productivity.

Concerning the collective well-being, a better recognition of non-team leader researchers and ITAs seems necessary. The establishment of working groups and a system for the review of ITA files by researchers other than the heads of staff eligible for promotion could help to create a feeling of transparency and equal treatment.

These suggestions are currently being implemented.

Recommendations regarding Evaluation Area 3: Scientific Production. p16

Keep up with an excellent scientific productivity and pay attention to technological and workforce needs for new joining young teams.

Although CIML has some means of leverage, that were used to attract 5 group leaders during the last mandate, it is mostly dependent on the will of governing bodies to support

adequately CIML development and young teams installation through technological and workforce allocation.

Recommendations regarding Evaluation Area 4: Contribution of Research Activities to Society. p16

Strengthen outreach activities towards the general public and/or patient organizations, by asking students to get involved in events for the general public.

This suggestion will be examined.

Specific point for CIML:

The Immunology teaching team, mostly constituted by AMU Professors and Maîtres de conférence working at CIML, deeply regrets that the current HCERES report completely failed to provide an evaluation of their activities, that would have represented a recognition of their important role in the CIML community. Their teaching activities are completely necessary for the excellence and recognition of CIML, as a leading research institute, notably through the formation of the next generations of Immunologists while providing CIML with a talented school of students, that contribute to the outstanding scientific production of the institute. Given the public nature of this report, it would have been important that their function is also associated to CIML success.

Specific answers from the research teams:

Equipe Roulland-Nadel (12)

Weaknesses and risks linked to the context (S. Roulland / B. Nadel's team): 'Funding for several projects will expire in 2022 or get extinguished with the departure of Dr Payet-Bonnet', ….

Current lab projects are funded through 2024-2025 and the departure of D. Payet represents <10% of the total team funding per year (only one active grant of 100k). Thereby, her departure is not expected to affect the financial wellness of the team.

Equipe Milpied (11)

1. *The description of the themes of the team is partial, limited to one past axis of research and one past axis of technology development. To summarize very briefly, as mentioned in my report and in my presentation to the evaluation committee during their site visit, my team focuses on understanding the functional plasticity of B cells through 4 research axes: (axis 1) single-cell and spatial transcriptomics technology and data analysis, (axis 2) basic germinal center B cell biology in humans and mouse models, (axis 3) functional plasticity of malignant lymphocytes in human lymphoma, and (axis 4) solid tumor-infiltrating B cells.*
2. *The team has produced more publications than stated in the report in high and mid-impact journals in which the team leader is first, (co-)last, or (co-)corresponding author: 1 Nat Immunol (Milpied et al. 2018, first and co- corresponding author), 1 Immunity (Gregoire et al. 2022, co-corresponding author), 1 J Hepatol (Renand et al. 2020, co-last author), 1 Front Immunol (Attaf et al. 2020, last author), 1 Adv Immunol (Milpied et al. 2021, first author), 1 Eur J Immunol (Attaf et al. 2021, last author).*

Equipe Pierre (14)

Weaknesses and risks linked to the context:

Most of the original articles issued by the team are signed by the team leader as a last author. ….

It is important for the younger permanent staff to gain in visibility by taking the lead on published original articles, as an asset for the future.

We are surprised by this comment and recommendation, since other permanent members of the team, signed most original articles of the team either as co-leading author (E. Gatti), unique last author (E. Gatti) or corresponding author (R. Argüello). They also have the opportunity to apply as principal investigator to ANR grants and EU grants.

Equipe Sieweke (16)

- Lena Alexopoulou joined the team in 2019, not 2016

- Contrary to what is stated, 2 new students (Lucas Raffinatto and Yann Groult) have joined the team in October 2022.

- We would like to point out that we had a clear governance structure with joint responsibilities of Michael Sieweke and Sandrine Sarrazin. Direction was further assured by frequent presence on site of Michael Sieweke, as well as regular online meetings and individual tutoring, drawing from a long experience of leading an international lab on two physical sites

- The Sieweke lab at TU Dresden will continue to be associated with CIML through an international research project (IRP) led on the Marseille side by Sandrine Sarrazin, integrating another CR (Berengere Delaval), 2 students and 2 ITA, who will be associated with the Toby Lawrence lab. This will in particular create synergies of the Lawrence and Sieweke lab for research in cancer immunology.

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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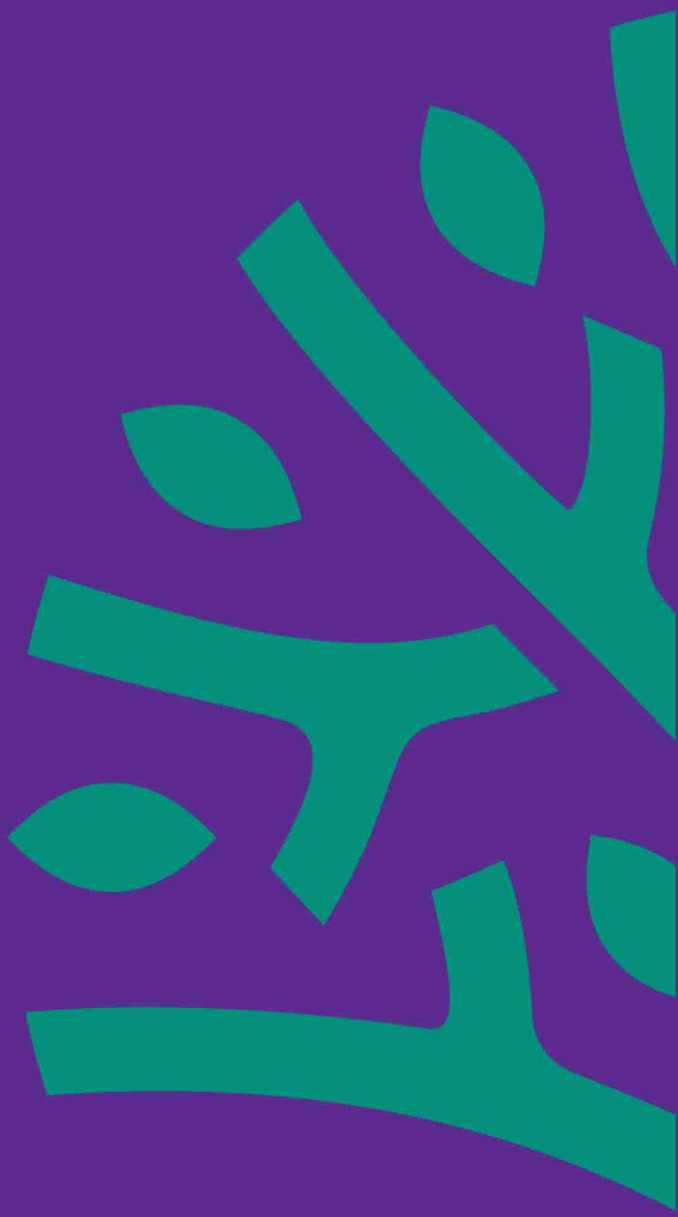

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