

EVALUATION REPORT OF THE UNIT
Chimie et biologie de la cellule

UNDER THE SUPERVISION OF THE
FOLLOWING ESTABLISHMENTS AND
ORGANISMS:

Institut Curie,
Centre national de la recherche scientifique -
CNRS,
Institut national de la santé et de la recherche
médicale - Inserm,
Université Paris sciences et lettres - Université PSL

EVALUATION CAMPAIGN 2023-2024
GROUP D

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In the name of the expert committee :

Gilles Guichard, Chairman of the committee

For the Hcéres :

Stéphane Le Bouler, acting president

Pursuant to Articles R. 114-15 and R. 114-10 of the Research Code, the evaluation reports drawn up by the expert committees are signed by the chairmen of these committees and countersigned by the President of Hcéres.

To make the document easier to read, the names used in this report to designate functions, professions or responsibilities (expert, researcher, teacher-researcher, professor, lecturer, engineer, technician, director, doctoral student, etc.) are used in a generic sense and have a neutral value.

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 Gilles Guichard, CNRS - Centre national de la recherche scientifique, Pessac

Experts:

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Mr Thierry Galli, Inserm

Mr Christophe Giraud, CNRS

Ms Sandrine Sagan, INC

Mr Arnaud Tourin, Université Paris Sciences & Lettres

Ms Tatiana Malherbe, Institut Curie

CHARACTERISATION OF THE UNIT

- Name: Cellular and Chemical Biology
- Acronym: CCB
- Label and number: U1143 Inserm – UMR3666 CNRS
- Number of teams: 3
- Composition of the executive team: Mr. Ludger Johannes, Unit Director; Christophe Lamaze, Deputy Director

SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement

SVE3 Molécules du vivant, biologie intégrative (des gènes et génomes aux systèmes), biologie cellulaire et du développement pour la science animale

THEMES OF THE UNIT

Research within The Cellular and Chemical Biology (CCB) unit aims at addressing fundamental questions in cell biology within an interdisciplinary research environment by integrating tools and concepts in physics and chemistry. CCB is composed of three teams: Endocytic Trafficking and Intracellular Delivery, Membrane Dynamics and Mechanics of Intracellular Signalling, and Chemical Biology. Research areas cover epitranscriptomics, metabolomic programming, inflammation, cellular plasticity and signalling, membrane organisation and trafficking, immunotherapy of cancer and infectious disease. Besides the primary goal to understand molecular mechanisms that regulate fundamental cellular processes, the unit also capitalises on acquired knowledge to develop new therapeutic approaches using disease-relevant models with a marked focus on cancer biology. Here is an overview of some representative research activities of the unit:

- function of glycans at the cell surface in endocytosis
- therapeutic exploitation of glycolipid-lectin driven endocytosis
- characterisation of caveolae mechanosignaling
- transmembrane receptor dynamics and signalling
- elucidation of receptor mediated metal endocytosis pathway regulation of cell state transition
- development of drug-like molecules triggering ferroptosis of cancer cells

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The unit was created in 2014 and composed of three teams with a focus on chemical biology of membranes. In 2015, a new team joined the unit expanding further the expertise in chemical biology and cancer biology. The unit was recreated on January 1, 2019 comprising three teams because of the retirement of one of the previous team leaders. The Cellular and Chemical Biology unit is located on the Paris campus of the Research Center of Institut Curie. The teams were initially located on two sites within a walking distance (i.e. the 1st floor of the Burg building and the 4th floor of the Trouillet building). Since 2021 and the renovation of the 5th floor of the Trouillet building, all the researchers of the research unit are located in the same building (4th and 5th floors of the Trouillet Building).

RESEARCH ENVIRONMENT OF THE UNIT

The Cellular and Chemical Biology unit is one of the thirteen research units (1,100 people) that constitute the Research Center of Institut Curie led by Pr Alain Puisieux since 2019. The Research Center, which includes a Translational Research Department, houses nineteen technology platforms organised as the CurieCoreTech and the CCB unit is involved in two of these (Chemical library / Metabolomics & lipidomics). Research activities within the Research Center encompass cell biology, genetics, epigenetics, immunology, soft matter physics, organic and medicinal chemistry.

Over the period under review, CCB has participated in several PIA (Programme d'Investissements d'avenir) including the LabEx Cell(n)Scale "From molecules to Tissues : where Physics & Chemistry meet Biology", the PSL Q-Life Institute (Institut de Convergence) which supports research and innovation for quantitative biology and the "SIRIC Institut Curie" which focuses on resistance to anti-cancer treatment. The unit is also involved in 'Institut Carnot Curie Cancer' which support innovation programs.

UNIT WORKFORCE: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	5
Chargés de recherche et assimilés	9
Personnels d'appui à la recherche	35
Sous-total personnels permanents en activité	49
Enseignants-chercheurs et chercheurs non permanents et assimilés	9
Personnels d'appui non permanents	0
Post-doctorants	37
Doctorants	9
Sous-total personnels non permanents en activité	55
Total personnels	104

DISTRIBUTION OF THE UNIT'S PERMANENTS BY EMPLOYER: in physical persons at 31/12/2022. Non-tutorship employers are grouped under the heading "others".

Nom de l'employeur	EC	C	PAR
INSTITUT CURIE	0	1	9
INSERM	0	5	3
CNRS	0	2	5
Total personnels	0	8	17

GLOBAL ASSESSMENT

During the evaluation period, the CCB unit has strengthened a trajectory of excellence in several key areas of cell biology, and chemical biology, while increasing further its visibility in the field of cancer biology.

-Organisation. The unit benefits from an exceptional environment within the Research Center of Institut Curie with access to state-of-the-art scientific facilities. During the period, the unit has consolidated its research premises and has contributed to expanding the CurieCoreTech network by creating a new platform in metabolomics and lipidomics. The unit is highly dynamic and perfectly integrated on site (multiple collaborations with other research units including UMR144, UMR168, U830, U900, and U932) and in its local environment (participation to six PIA projects). In 2021, the consolidation of its premises was achieved (Trouillet building) and the part of the unit in the Burg building could finally move to the newly refurbished fifth floor in the Trouillet building.

-Attractiveness. The recruitment of promising young researchers (five) /engineers (five) with long-term positions over the period, the numerous prizes and distinctions awarded to the team leaders (including the Klaus Grohe Prize and the Tetrahedron Young Investigator prizes, the Grand Prix from National Academy of Pharmacy, election as a member of the German Academy of Science — Leopoldina), the organisation of 22 international meetings (including Embo, Jacques Monod, Tetrahedron conferences and PSL Chemical Biology Symposium) and the many successes achieved in competitive calls from national and international agencies (Mizutani Foundation for Glycoscience, H2020 MSCA, ERC POC, thirteen ANR contracts, la Fondation pour la Recherche Médicale, la Ligue contre le Cancer, Fondation ARC) which represent 85% of the total 9,843 k€ obtained during the period, collectively attest to the extraordinary attractiveness of this research unit.

-Production. The unit is developing a research of excellence at the highest international level, being a pioneer in several research areas such as endocytosis and chemical glycobiology, mechanobiology, receptor signalling, metal endocytosis and small molecule inducers of ferroptosis, which is reflected in its exceptional scientific

output over the period both quantitatively (139 papers over the period out of which 60 as last or co-last authors) and qualitatively with >30 papers in major (multi)disciplinary science journals (*Nature*, *Science*, *Cell*, *Nat Chem*, *Cancer Discov*, *Nat Cell Biol*, *Nature Commun*, *Nature Chem Biol*, *JACS*, *ACIE*).

Some important scientific achievements:

- The discovery of a CD44-mediated iron endocytosis pathway that regulates cell state transitions in cancer and immune cells is remarkable (team 3).

- The discovery that caveolae play a key role in muscle cells, linking mechanical signals to intracellular signalling, and that mutations in Cav3 can cause clinical symptoms in dystrophic patients due to the loss of this function (team 2).

- Major results from team 1 devoted to new concepts of glycoprotein endocytosis (i.e. GlycoSwitches).

-Outreach. The CCB unit has made remarkable contributions to society through its research activities first but also by the quality and quantity of its non-academic interactions. In particular, the unit has been extremely successful in combining cutting-edge fundamental research with diversified technology transfer activities, including the filing of fifteen patent applications, collaborative agreements (OGD2 Pharma), commercialisation of products (by ProbeChem and Sigma-Aldrich), and the creation of start-ups (e.g. Metal Therapeutics). Furthermore, the participation in outreach programs and strong public engagement including radio appearances (France Inter, France Culture, RTL) and coverage in national newspapers such as *Le Monde* demonstrate an exceptional commitment to share knowledge and contribute to the high visibility to the unit.

In the context of its trajectory and to further strengthen its leading position at the interface between chemistry and cancer biology, the unit proposes to reorganise and expand its size by bringing in new teams with additional and complementary expertise. This project which seeks to maintain an equilibrium between chemistry and biology clearly underlines the exceptional dynamism and ambition of the CCB unit.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The recommendations in the previous report have all been taken into account.

-With regard to the recommendation to recruit a permanent assistant professor at the interface between biology and chemistry in order to strengthen interactions between the unit and neighbouring universities, two recruitment campaigns were organised but were unsuccessful due to a lack of candidates meeting the expected criteria. A third campaign could not be carried out due to the Covid pandemic and the renovation of the premises. The recruitment campaign was finally postponed in view of the project to create the Center for Chemical Biology of Cancer (CBC) proposed for the next period as stated in the unit's trajectory.

-There was a concern of keeping the expertise in chemistry despite the mobility and retirement of three engineers and researchers. The chemistry engineer positions have all been maintained over the period, though the chemistry researcher position still has to be replaced. Several options are considered including the recruitment of additional chemical biology teams in the context of the future Center for Chemical Biology of Cancer (Unit Trajectory). The recommendation to maintain an equilibrated ratio between Postdocs and PhD students has been taken into account (currently 7 postdocs and 10 PhD students in the unit) and the unit has trained 23 PhD students over the period.

-The recommendation regarding lab space optimisation has been solved with the renovation of the premises in the building "Trouillet", which resulted in a slight increase of the overall space allocated to the unit (431 m²).

B - EVALUATION AREAS

Considering the references defined in the unit's evaluation guidelines, the committee ensures that a distinction is made on the outstanding elements for strengths or weaknesses. Each point is documented by observable facts including the elements from the portfolio. The committee assesses if the unit's results are consistent with its activity profile.

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

Assessment on the scientific objectives of the unit

The CCB unit has established a highly competitive research program in cellular and chemical biology with clear and timely scientific objectives. These ambitious goals have been realised through effective fundraising efforts at local (6 PIA projects e.g. LabEx PSL Q-Life), national (ANR, INCa, and charities), and international levels (e.g. ERC POC, Cefipra), robust collaborations among the three groups leaders, and both within the Curie units (UMR144, UMR168, U830, U900, and U932) and worldwide (Europe, USA, India). Furthermore, the unit has demonstrated its proficiency in enhancing the value of its fundamental research through a very proactive patent filing policy which remarkably led to the creation of a spin-off company (Metal Therapeutics).

Assessment on the unit's resources

Despite its modest size (43.5 personnel), the CCB unit maintains a well-balanced composition of permanent/contract staff (47%/53%), researchers (11)/technical personnel (55%/45%), and doctoral(11)/postdocs (7). It has effectively managed to secure a budget of nearly €10 million euros over the specified period, with 85% of funding secured through competitive grants (ERC, Cefipra, ANR, FRM, ...) and also industrial contracts (OGD2 Pharma, Servier). Since 2021, the unit has benefited from consolidated laboratory premises, and more generally it also has access to state-of-the-art scientific facilities, including highly competitive platforms within the Research Center of Institut Curie.

Assessment on the functioning of the unit

Being embedded within the Research Center of the Institut Curie, the CCB unit benefits from specific and well-defined operational practices and tools designed to drive continuous improvement on important issues such as gender equality, staff training, Health and safety protocols, and data management. Substantial efforts have been conducted over the period on the reorganisation of the laboratory space including the relocation of half of the unit's personnel into new premises, and substantial update of security standards in chemistry laboratories. Decisions are made collegially by the three team leaders with the advice of unit members when necessary to ensure efficiency, and discussed at the unit council.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

The CCB unit as a whole has established distinctive, ambitious and timely scientific objectives, some of which, with well identified prospects in terms of clinical potential and technology transfer. The areas where the unit has excelled, and which led to pioneering international work over the period, include endocytosis of membrane glycoproteins, caveolae mechanics, interferon-gamma signalling, mechanisms of metal uptake, chemical control of cell-state. Although it is clearly a high risk – high gain situation, many objectives appear to be well within reach in light of the unique expertise developed by each team in the unit and between teams (as shown by joint papers, e.g. ACIE 2022, Nat Chem Biol 2020, Nat Commun 2019, J Cell Biol 2018). The unit is well integrated in the Research Center of the Institut Curie and in its local environment. This is evidenced by the creation of one platform with expertise in metabolomics and lipidomics, now belonging to the CurieCoreTech network and by the acquisition of unique microscopy instruments such as the lattice light-sheet microscopy instrument) that serves key research projects. Moreover, the unit participated to six PIA projects (e.g. LabEx, PSL Q-Life) over the period, with all teams belonging to such excellence networks. Regarding the unit management, decisions are made collegially by the three team leaders with the advice of unit members when necessary to ensure efficiency. All three teams have managed to make new recruitments (both staff researchers and engineers) over the period, a sign of the dynamism of the unit. Although the research conducted by the three teams predominantly focusses on fundamental aspects, the team leaders have successfully exploited the results for potential transfer whether through patents (x15 filed patents over the period), collaborative agreements, or by creating innovative start-ups (i.e. Metal Therapeutics).

Weaknesses and risks linked to the context

No weaknesses were notified by the committee.

2/ The unit has resources adapted to its activity profile and research environment, and makes use of them.

Strengths and possibilities linked to the context

With 43.5 personnel in total (out of which 11 staff researchers, 8 staff engineers and 1.5 administrative personnel with long-term positions), the unit is modest in size, but nevertheless, it has shown a remarkable ability to generate resources to support its activities. Excluding staff salaries, the unit has been doing extremely well in terms of funding, with 85% of the total 9,843 k€ obtained during the period, resulting from successes to competitive calls. This allowed the teams to recruit personnel with temporal positions including PhDs, postdocs and engineers, amounting for more than half of its workforce (53% temporal positions). In 2021, the unit achieved its consolidation by relocating one part from Burg building to the newly refurbished 5th floor in the Trouillet building, the rest of the unit being already located on the 4th floor of the same building. These premises are equipped with fume hoods and are compatible with the activities in organic synthesis of part of the unit. This move to a single building should make life easier for the unit.

Weaknesses and risks linked to the context

Despite the dedicated effort of the current administrative personnel in the unit, potential challenge may arise from the limited 1.5 FTE in the administrative department of the unit.

3/ The unit's practices comply with the rules and directives laid down by its supervisory bodies in terms of human resources management, safety, the environment, ethical protocols and the protection of data and scientific heritage..

Strengths and possibilities linked to the context

Being a member of the Research Center of the Institut Curie, the unit benefits from plans and supports on working conditions, human resources, and health and safety issues. In line with the Gender Equality, Diversity and Inclusion Plan (GEDIP) of the Research Centre of Institut Curie, the unit has put in place an impartial recruitment process based on candidates' qualifications. In terms of training, the unit personnel has access to doctoral programs, international scientific courses, seminars and symposia at the Institut Curie research centre, as well as training on the use of equipment and on scientific integrity. In addition, the unit's staff have taken part in 55 training programs distributed in five categories: Health and Safety (H&S), Science, management, institutional and personal development. In terms of H&S, the unit has two prevention assistants. During the period, it has taken specific measures to improve safety in chemical laboratories. An apprentice specialising in quality, safety and the environment spent a year in the unit, preparing a complete inventory of all compounds and improving storage conditions by grouping chemical and pharmaceutical products and documenting associated risks. For the management of large amount of the data generated, the unit benefits from the support of the Data Office created in 2017 at the Institut Curie.

Weaknesses and risks linked to the context

The gender balance amongst the scientific staff is slightly unbalanced with 39% women, and 61% men. The unit is fully aware of this imbalance and remains vigilant. One way to redressing this imbalance as proposed by the unit is to promote the underrepresented gender among applicants of similar merit when making new recruitment. The unit did not provide specific information on its position with regard to energy and resource saving, particularly in terms of travel management and waste treatment, for example.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The reported indicators underscores the exceptional attractiveness of the unit. The recognition of the teams for their pioneering research work as evidenced by the numerous awards received by the group leaders (e.g. Tetrahedron Young Investigator Award, Grand Prix de l'Académie nationale de pharmacie), and their role in structuring and energising the community is outstanding. This attractiveness can also be measured by the ability to secure highly competitive funding (ANR, Inca, FRM, ...) as well as by the substantial influx of five new permanent researchers who have joined the unit. Significant efforts have been dedicated to acquiring cutting-edge equipment for live cell imaging and establishing the metabolic and lipidomics platform.

1/ The unit has an attractive scientific reputation and is part of the European research area.

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

3/ The unit is attractive through its success in competitive calls for projects.

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

Strengths and possibilities linked to the context for the four references above

1/ The unit has demonstrated and continues to demonstrate a remarkable level of attractiveness that is manifested according to all four standards. These include substantial contributions to prestigious conferences and the successful organisation of 22 events including major events such as Embo and Tetrahedron Conferences in biology and chemistry. Furthermore, the group leaders carry editorial responsibilities for eight well-established journals (among which ChemBioChem, ACS Chem Biol, Traffic, Biol cell, Bioorg Med Chem, PLoS One, Sci. Rep.), are members of esteemed academic institutions and organisation like the Royal Society of Chemistry, the National Order of Merit, the German Academy of Science (Leopoldina), and the European Molecular Biology Organisation (Embo) and have received a substantial collection of awards (Tetrahedron Young Investigator Award, the Grand Prix from the National Academy of Pharmacy) that reflect the recognition and appreciation of the whole scientific community.

2/ The unit benefits from an environment at the Research Center of Institut Curie that facilitates the integration of new personnel including young researchers, notably by funding young researchers to attend conferences. Other measures from the unit include the involvement of PhD students in the organisation of meetings, such as the PSL chemical biology conferences. Attractiveness is also illustrated by the number of young researchers (x5) who obtained a permanent position (3 Inserm, 1 CNRS, 1 Univ) within the unit during the period.

3/ The unit has achieved remarkable success in securing competitive funding, with a substantial budget of €8.3 million over the designated period. This funding has been sourced from both international entities, such as H2020, and national bodies like ANR and INCa. Additionally, a substantial number of contracts have also been acquired from charities (FRM, La Ligue, and Fondation ARC) as well as regional sources and private companies. It is important to note that all three teams did equally well in getting almost the same amount of funding during the contract period. These competitive funds have played a crucial role in financing temporary positions, specifically supporting 26 postdoctoral researchers, 23 PhD students, and ten engineers over the period, among which a large fraction were recruited from abroad (13 different nationalities).

4/ Finally, during the period the unit has remarkably developed and expanded research equipment and technological skills. This is exemplified by the state-of-the-art 'Metabolomics and Lipidomics' platform launched by a former postdoc of the unit and led the PI of team 1, and the acquisition of cutting-edge mass spectrometers alongside with the development of collaborations and industry partnerships (OGD2 Pharma). Finally, the acquisition of a second lattice light sheet microscopy emphasises the unit leadership in live cell imaging technologies and creates a favourable environment for cutting-edge developments in quantitative biology. These developments have also led to the creation of a new team (Sairpico, April 2023) with expertise in artificial intelligence and computer science for cell biology, in collaboration with Inria in Rennes.

Weaknesses and risks linked to the context for the four references above

No weaknesses were notified by the committee.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The production of the unit in the fields of chemical biology, cell and cancer biology is outstanding as reflected first by the publication of major primary research papers and reviews in the most prestigious journals (Nature, Sciences, Nat Commun...); with members of the unit being last or co-last authors on 60 out of 139 papers. Noteworthy, each team has actively contributed to the scientific output of the unit. PhD students and postdocs consistently published papers during their time in the unit and engineers are systematically included as coauthors on publications to which they have contributed. Moreover, the unit demonstrates a strong commitment to scientific integrity, ethics, and open science, as evidenced by their proactive approach combined with that of the Research Center of Institut Curie.

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

2/ The unit's scientific production is proportionate to its research potential and properly shared out between its personnel.

3/ The scientific production of the unit complies with the principles of research integrity, ethics and open science. It complies with the directives applicable in this field.

Strengths and possibilities linked to the context for the three references above

1/ The scientific production of the CCB unit is outstanding. The unit has made a substantial impact on the international scientific community in chemical biology as well as in cell and cancer biology by publishing a number of primary research articles and reviews in the most prestigious international journals such as *Nature*, *Science*, *Cell*, *Nat Chem*, *Cancer Discov*, *Nat Cell Biol*, *Nature Commun*, *Nature Chem Biol*, *JACS*, *ACIE*. This leading contribution is visible by the number of papers as last or co-last authors (60 among the 139 papers published since 2017). The discovery of a CD44-mediated iron endocytosis pathway that regulates cell state transitions in cancer and immune cells (by team 3) is remarkable. Another remarkable result (by team 2) is the finding that caveolae play a key role in muscle cells, linking mechanical signals with intracellular signalling and that Cav3-associated mutations may cause clinical symptoms in dystrophic patients due to the loss of this function. The quality of the scientific output is also highlighted by major results by team 1 dedicated to new concepts in glycoprotein endocytosis, (i.e. GlycoSwitches) currently under evaluation for publication and selected as part of the portfolio of the unit.

2/ It is noteworthy that the distribution of the scientific output among the three teams is well balanced, with each team actively contributing to the research of the unit. The practice of including engineers as coauthors on publications to acknowledge their contributions is noteworthy. Another positive sign is the fact that all PhD students and postdocs have been publishing papers during their stays within the unit. 3/ The unit and the research centre of the Institut Curie demonstrate a strong commitment to scientific integrity, evident from their proactive initiatives, such as workshops and signing the French Charter of Ethics, as well as their establishment of a scientific integrity board and officer in 2021. Additionally, their ethical approach to handling patient material and laboratory animals includes obtaining necessary authorisation, seeking informed consent, and maintaining rigorous oversight for studies involving these subjects.

Weaknesses and risks linked to the context for the three references above

No weaknesses were notified by the committee.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The unit has made outstanding contributions to society through its research activities and by the quality and quantity of its non-academic interactions. With the aim to translate scientific discoveries into practical applications, the unit has been actively engaged in technology transfer, patent filings (15), as well as the creation of spin-off biotech companies (Metal Therapeutics) and commercialisation of research products (e.g. by Sigma Aldrich). These contributions are truly impressive. Furthermore, the participation in outreach programs and strong public engagement including appearance on National Radios (France Culture, France Inter, RTL) and TVs (TMC) as well as articles in well-known national newspapers (e.g. Le Monde for team 3) demonstrate an exceptional commitment to share knowledge and contribute to the high visibility to the unit.

1/ The unit stands out for the quality and the amount of its interactions with the non-academic world.

2/ The unit develops products for the cultural, economic and social world.

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

Strengths and possibilities linked to the context for the three references above

Through the diversity of its non-academic interactions, the research unit has demonstrated a remarkable ability to bridge the gap between scientific research and society. First, the unit is actively engaged in technology transfer and patent filings in the field of cancer treatment and diagnosis and infections (15 deposited), demonstrating a strong commitment to translate their research into practical applications. The creation of spin-off biotech companies like Metal Therapeutics and the option for collaboration with OGD2 Pharma highlight this potential to contribute to advances in cancer treatments and diagnostic. The commercialisation of products like Ironomycin by ProbeChem and Retro-2 by Sigma-Aldrich is another example of this excellent contribution to the economic world. In terms of public outreach, Raphaël Rodriguez's extensive engagement with various media outlets, including "Le Monde", "France Inter", "France Culture" and a round-table with French President Emmanuel Macron are just outstanding and exemplify a strong commitment and a remarkable ability to sharing scientific knowledge with the general public. Participation of members of the unit in programs like "Declics" more specifically dedicated to a younger audience add another dimension to this engagement.

Weaknesses and risks linked to the context for the three references above

No weaknesses were notified by the committee.

ANALYSIS OF THE UNIT'S TRAJECTORY

During the last period, the CCB unit and its three teams have shown their ability to work together in a demanding interdisciplinary environment that combines chemistry and biology to carry out cutting-edge research in the field of cell biology. The proposed unit's trajectory building on this success is notably ambitious. It aims to advance research in chemical biology, fundamental cell biology, and cancer within a clinical context while maintaining the elevated scientific standards and the high degree of interdisciplinarity that characterises it. To achieve this objective, the unit has chosen to expand its size by bringing in new teams with additional and complementary expertise in areas such as chemical biology, the tumour microenvironment, and mechanisms of drug resistance, clinical research as well as computational biology and image analysis. The unit will be renamed "Chemical Biology of Cancer" (CBC) Unit and will comprise ten teams with 112 staff (about 2.5-fold increase), with two additional teams in chemical biology, one of which has yet to be recruited. This project clearly underlines the exceptional dynamism and attractiveness of the CCB unit, which will be strengthened by teams that are international leaders in their respective fields. The head of the "Stress and cancer" team, will be the new unit's director. This project is strongly supported by the head of the Research Center of Institut Curie. On one hand, introducing new team leaders in chemical biology and cancer biology will facilitate the exploration of new directions and could lead to advances, including the discovery of new mechanisms for combatting cancer and their translation into clinical applications. On the other hand, the structure of the new unit will be substantially different from the current one, and care should be taken not to compromise the existing dynamism and synergies within the CCB unit.

Several challenges have been identified along the way. First in terms of the unit's location, a single facility is necessary to encourage inter-team cooperation and to foster links, a goal which can only be achieved through the construction of the new building. Secondly, it is important to maintain a good balance between chemistry and biology, and recruiting new chemistry teams is essential for the success of the project. Finally, care will need to be taken about the administrative resources supporting the unit, as the current staff may struggle to cope with the anticipated increase in the unit's size.

RECOMMENDATIONS TO THE UNIT

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

The CCB unit has developed a remarkable environment for first-class research in cellular and chemical biology, achieving ambitious goals through effective organisation and networking, competitive national and international fundraising, robust collaborations among the three teams, the acquisition of cutting-edge instruments and the creation of new platform. The recommendation that can be made to the unit is to maintain this degree of commitment and excellence and to ensure that it will preserve this successful ecosystem. The whole unit is now housed in the same building, and it is recommended to maintain such a cohesive environment when considering the future of the unit. With this in mind, considering the relocation of the Metabolomics and Lipidomics platform to the Paris site could certainly prove advantageous for a number of research projects. Finally, in the context of the unit's trajectory, addressing the current understaffing challenge in the administrative office is essential, as well as further enhancing chemistry expertise through the recruitment of new teams. It is also important for the management team to communicate extensively with its staff in preparation for the substantial changes proposed in the new trajectory.

Recommendations regarding the Evaluation Area 2: Attractiveness

The attractiveness of the unit is exceptional and one obvious challenge is to sustain this high standard. There is no doubt that the teams have ongoing projects and results that ensure them to stay highly competitive within their respective fields, especially when seeking funding from international agencies. Strengthening the expertise of the unit in quantitative biology through the recent recruitment of a new team will undoubtedly create new opportunities to increase attractiveness and competitiveness. As a sign of its attractiveness, the unit has demonstrated remarkable ability to attract talented young researchers and help them in securing stable positions. This effort should persist as part of the unit's new trajectory with particular attention to maintaining equilibrium across disciplines.

Recommendations regarding Evaluation Area 3: Scientific Production

The scientific output reflects the pioneering research work from the three teams over the period and underscores the complete scientific coherence within the unit. There is not much to add than to encourage the unit to sustain this high standard in terms of scientific production.

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

The success of the unit's nonacademic interactions, particularly in technology transfer and public outreach is outstanding and there is little recommendation to make. As technology transfer is certainly an area that may interest some young researchers within the unit, there is an opportunity here to actively engage them more specifically in this direction.

TEAM-BY-TEAM OR THEME ASSESSMENT

Team 1: Endocytic Trafficking and Intracellular Delivery

Name of the supervisor: Mr. Ludger Johannes

THEMES OF THE TEAM

The Endocytic Trafficking and Intracellular Delivery team focus in the molecular mechanisms of the function of glycans. Pioneer work from the team established a mechanistic proposal according to which glycan binding proteins transduce the complexity of glycan structures into membrane mechanical signals implicated in the formation of endocytic pits, termed the GlycoLipid-Lectin (GL-Lect) hypothesis. In this context, the team work encompasses mechanistic, functional and therapeutic aspects of the GL-Lect hypothesis.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

In the previous Hcéres evaluation, it was recommended that the team strengthen their expertise in chemistry on the long-term by the integration of one expert team. In the current report, the team has identified the retirement of one PI as a current threat that weakens the organic chemistry expertise of the team. Current efforts of the team to address this issue include the request for an engineer (IR) position and ongoing discussions with a senior chemical-biology postdoc that might be interested in joining the team for a staff scientist position.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	6
Sous-total personnels permanents en activité	9
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	2
Doctorants	3
Sous-total personnels non permanents en activité	6
Total personnels	15

EVALUATION

Overall assessment of the team

Team 1 pioneered original research concerning the GL-Lect hypothesis, have addressed many open questions in the field that resulted in an impressive list of outstanding publications (among which Cell 2017, Nat Chem Biol, 2020, ACIE 2021, Nat Commun 2019, 2020, 2021), the establishment of numerous collaborations (FMP Berlin, Lund Univ., Univ. Manchester, harvard Univ.) and consequent international (Mizutani Foundation for Glycoscience, ERC POC) and national (ANR, FRM, Ligue contre le cancer) financial supports (2'880 keuros). Major results from team 1 devoted to new concepts of glycoprotein endocytosis (i.e. GlycoSwitches). The team has proven their outstanding attractiveness at national and international level via several indicators (Elected member of the German National Academy of Sciences — Leopoldina, Elected member of the European Molecular Biology Organisation (Embo), President of Jacques Monod meeting...). Their work is an excellent example of the remarkable successful balance between fundamental and translational research resulting in contract collaborations with biotech companies (OGD2 Pharma SAS), commercialisation of products (Retro-2 by Sigma-Aldrich) and upcoming promising novel therapies against tumours and infections.

Strengths and possibilities linked to the context

The excellent attractiveness of the team can be appreciated in the facts therein mentioned. The team has attracted several young researchers (PhD students and postdoctoral researchers) that have been trained by the team. The excellent publication level of these young researchers during their stay in the team allowed them to find stable positions in industry or academia. The team has established excellent collaborations at the national and international levels that reflects in the excellent funding level obtained within the period (coordination of 2 ANR, partner in 6; coordinator of 1 INCa and partner in 1; partner is a Swedish Research Council grant; coordinator of an ERC grant finishing in 2024; etc.). The team leader is recognised for his work at the national and international level as evidenced by the number of invitations to national and international conferences (40 in the evaluation period including 3 Gordon and 4 Embo conferences) and seminars worldwide (USA, Australia, Denmark, India, etc.), the organisation of several conferences and strong implication in science administration. The international recognition of the team leader can also be appreciated by several honors that he has obtained, namely the fact that he is an elected member of the German National Academy of Sciences and the Embo organisation.

The team has an impressive list of outstanding publications since 2017. During the evaluation period, the team has published 49 research articles (14 published as last or co-last author) and nineteen reviews. Among the publications with first or last authorship by the team members, noteworthy one ACS Nano, one Nano Lett., one Nat. Chem. Biol., one Nat. Commun., one Angewandte Chemie. To note that among the review articles by the team, the review on J. Cell. Sci. has become a reference in the field with over 400 citations. The team also included in the portfolio two preprints (not yet uploaded into BioRxiv due to confidentiality reasons) addressing the GlycoSwitches project under review in Science as back-to-back submissions.

Regarding the contribution of the team research activities to society, it should be mentioned as an option on license and collaboration contract in place with a French Biotech company (OGD2 Pharma SAS) to exploit the Lectibody technology for neuroblastoma in children and several cancers in adults, namely breast cancer. In addition, a chemical approach has been pursued by the team (associated with 2 patents) to obtain a fully synthetic version of dendritic cell targeting and antigen delivery toolbox (STxB). The team plans to develop the STxB approach towards the clinics for mucosal vaccination against infectious diseases of the respiratory tract and mucosal oropharyngeal cancers. The creation of a new start-up company is envisioned.

Weaknesses and risks linked to the context

One of the immediate challenges that the team faces lies in the publication of the two GlycoSwitch manuscripts (presented in the portfolio) in high international visibility journals as aimed by the team. Such publications could be detrimental for the decision of the ongoing evaluation of the ERC synergy grant (final results to be known in November 2023) that will allow substantial financial support to maintain and amplify long-term team investments (mentioned below). Taking advantage of the previous ERC advanced grant (2014-2020), the team has opted for long-term investments in the fields of structural biology and *in vivo* biology, namely the acquisition of one of the first biology-dedicated lattice light sheet microscope in Europe (in 2016) and the purchase of a high-end Q-Exactive orbitrap mass spectrometer for Lipidomics (2017). The second acquisition was key for the creation of the metabolomics/lipidomics CurieCoreTech platform. The first lead to the creation of an Inria-Inserm team on space-time imaging, artificial intelligence and computing. The maintenance and support of these novel technologies requires substantial funds that the team and collaborators must obtain in upcoming years.

One threat already raised in the previous Hcéres evaluation and that the team mention the need to reinforce the organic chemistry expertise of the team following F. Schmidt retirement. The team has requested for an IR and ongoing discussions with a senior postdoctoral research are also underway. Organic Chemistry is a key discipline in ongoing team projects, therefore the lack of personnel in this domain presents a major threat for the team.

Main threats concerning the team contribution of research activities to society are those typically encountered in the field due to competitor strategies, access to investor funds and recruitment of motivated and experienced personnel.

Analysis of the team's trajectory

The team project for the next contractual period lies on GL-Lect hypothesis established by the team that proposes a mechanism that links together molecular factors (tumoral glycoproteins, glycolipids and galectins) in a process of non-conventional clathrin-independent endocytosis.

To continue along this line, the team has established 3 solid objectives for the next period that go from fundamental to translational research: i) study the mechanisms by which glycans (commonly viewed as being rather static) undergo unexpectedly acute changes (min time scales) to trigger GL-Lect driven endocytosis (termed GlycoSwitches); ii) understand pathophysiological functions of GlycoSwitches, and iii) therapeutically exploit knowledge on GlycoSwitches in cancer, infection, and lysosomal storage diseases. The realisation of the project relies on methodologies present in the team and collaborator's laboratories. Several contracts have started in 2022-2023 and will run up to 2027 (1 ANR, 1 ERC, 1 PEPR), ensuring the funds for the realisation of the projects. In addition, the team has received the label FRM (2022-2025) and associated funds that could help obtaining future financial support.

RECOMMENDATIONS TO THE TEAM

The scientific production and activities of the team are outstanding as well as the team attractiveness. Therefore, the committee encourages the team to continue on that sense. The acquisition by the team of new technologies in mass spectrometry and high-resolution fluorescence microscopy provides new tools important for the research conducted by the team, the institute and the scientific community in general. Such technologies should contribute to attracting additional users (via platform services) that could in part allow for the financial support needed for future maintenance.

The team is encouraged to continue their efforts towards finding a solution regarding the current lack in human resources in the field of organic chemistry. Such expertise is key in many projects conducted by the team and while collaborative work could in part temporarily solve the issue, the recruitment of personnel within the team will be instrumental.

Team 2: Membrane Mechanics and Dynamics of Intracellular Signaling
 Name of the supervisor: Mr. Christophe Lamaze

THEMES OF THE TEAM

This team studies the role of membrane dynamics and mechanics in the control of intracellular signalling. The first focus is on the spatial regulation of signalling by membrane traffic and membrane nanodomains. This team, a pioneer in the discovery of the signalling endosome, is elucidating the endosomal molecular mechanisms that control the specificity of sorting and signalling of INF- α and β receptors. The second axis is to characterise the mechanosignaling role of caveolae in cellular functions and pathophysiology. The team discovered a new function of caveolae (Cell 2011 with 780 citations), demonstrating that these invaginations of the plasma membrane are mechanosensors that respond to mechanical stress by flattening to maintain homeostasis and the integrity of membrane tension.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The only weakness mentioned in the previous report concerns the number of permanent researchers in the team. Indeed, in the previous period, the PI was only researcher of the team with a permanent position. Since 2020, one person has obtained an Inserm CRCN position in 2019 and now he is leading the axe 2 in the team.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	4
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	6
Doctorants	2
Sous-total personnels non permanents en activité	8
Total personnels	12

EVALUATION

Overall assessment of the team

The team carries out outstanding research in the field of membrane mechanosignaling, with major impacts in both fundamental and translational research.

The team's publication record is outstanding (17 primary research papers and 11 reviews including Nat Cell Biol 2022, 2023, Nat Commun 2019, 2020, Sci Adv 2022), as their national and international attractiveness and visibility (competitive funding amounting for 2'714 keuros over the period, Grand Prix from National Academy of Pharmacy in 2019, organisation of the first Embo Workshop on "Caveolae and Nanodomains" in 2019, international collaborations including with Rockefeller Univ, Manchester Univ, Univ Chicago, Weismann Institute). The major scientific achievements are the discovery that caveolae play a key role in muscle cells, linking mechanical signals to intracellular signalling, and that mutations in Cav3 can cause clinical symptoms in dystrophic patients due to the loss of this function.

Strengths and possibilities linked to the context

The PI is a world-renowned expert in the field of membrane trafficking and signalling, and his team has made major and completely unexpected discoveries. The synergy between the two researchers in the team is excellent and fruitful.

The scientific output is exceptional for the size of the team, which includes the DRCE team leader, one CRCN, one IR and one IE, three PhD students and four postdocs. four PhD students defended their thesis during the evaluation period. The team's articles are published in high quality journals; Nature Cell Biology 2023, Nature Communications 2019 & 2020 ; Science Advances 2022 ; Angewandte Chemie 2022. The team has been invited to write nine reviews in prestigious journals such as Current Opinion in Cell Biology, Traffic.

The team's projects are extremely original, using a combination of cutting-edge transdisciplinary experiments and prestigious national and international collaborations in the fields of chemistry and theoretical physics.

There is a strong synergy between the unit's teams. Synergy with the chemists in another team in the Unit has led to the identification of interferon inhibitors, resulting in an article in Angewandte Chemie and a European patent in 2021. This project therefore has translational application and prematuration contract were obtained.

The team has established excellent national and international collaborations that led to major discoveries published in excellent journals (Nature Cell Biology 2023, Advanced Science 2022, Nature Communications 2019, Developmental Cell 2019, Human Molecular Genetics 2018).

The team obtained funding of excellence (international, European and national), with 3 INCa contracts, 5 ANR contracts, 1 Fondation ARC label and 1 Cefipra collaborative contract with India obtained by the PI. The CRCN in the team obtained 2 contracts over the period (Ligue Régionale and Fondation ARC). Over the period, the team obtained 2714K€.

The team has an excellent national and international visibility and contributes to the spreading of French research at the international level. This is evidenced by the number of citations of their articles (over 10,000) and the number of invitations to international conferences (15 since 2017). The PI has organised 3 international conferences (including the first Embo workshop on "caveolae and nanodomains"), has been invited to international conferences (such as 2 Embos, 2 GRCs, 2 key notes) and to 21 seminars. In 2019, the PI received the Grand Prix de L'Académie Nationale de Pharmacie.

The PI is involved in research administration (2 terms on the Inserm Scientific Council, chairman of the Inserm electoral commission that set up the CSSs, member of the Inserm joint administrative commission), research evaluation (member of the Ligue, ARC, Institut Pasteur, FRM commissions, participation in 15 thesis juries, 4 HDRs). The PI teaches in France and at foreign universities (Chile and Argentina).

Weaknesses and risks linked to the context

There is no weakness per se to mention, except the one raised by the team itself regarding the difficulty to attract postdoctoral fellows.

Analysis of the team's trajectory

The team's projects are a continuity of the major discoveries they have made in the field of mechanobiology. They propose a new paradigm with the existence of remote control of caveolin-1 complexes that form following the disassembly of caveolae on structures such as focal adhesions. They propose to characterise these caveolin-1 assemblies with nanometric resolution in relation to membrane tension, to elucidate the molecular mechanisms of the remote control that these complexes exert on focal adhesions and then, using intestinal cells in spheroids, to study this remote control mechanism in this three-dimensional context. The project on interferons will analyse how the nanometric organisation of the plasma membrane and the interaction of receptors with lipids responds to mechanical forces, forces that are a key event in the tumour environment.

State-of-the-art microscopic techniques, as well as in vitro systems (GUV) and biophysics, will be used to answer these mechanobiological questions.

RECOMMENDATIONS TO THE TEAM

The team has a world-leading position in their two research lines, their publication record is outstanding and their visibility excellent. The team is encouraged to follow the same line and to keep this dynamism and excellence in the field.

The two permanent researchers have assumed an excellent leadership.

As has been successfully done in the past, this team must continue to collaborate with the unit's teams.

Team 3: Chemical Biology
 Name of the supervisor: Mr. Raphaël Rodrigez

THEMES OF THE TEAM

The team benefits from a worldwide recognition in drug targeting of metal homeostasis and signalling pathways to modulate or target cell states with clear impact on drug development in cancer and inflammation. The use of small compounds and click chemistry to evaluate potential therapies and identify new targets for clinical intervention is a distinctive character and a strong asset of the team that masters both chemical biology and cell biology.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

"Increase PhD training"

This point has been taken into consideration with six supervised PhDs during since 2017 and one HDR that will further increase the supervision capacity of the team.

"would benefit from attracting a permanent scientist to support current and future activities"

Several recruitments (2CRCN and 2 IR) during the current period have strengthened the team.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	5
Sous-total personnels permanents en activité	7
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	5
Sous-total personnels non permanents en activité	6
Total personnels	13

EVALUATION

Overall assessment of the team

The team has an exceptional international outreach in terms of academic appeal (as illustrated by an impressive list of awards including the Liliane Bettencourt Prize for Life Sciences in 2023, the distinction of Knight of the National Order of Merit, the Tetrahedron Young Investigator Award in 2019) and scientific production (35 primary research papers and 12 reviews in leading journals among which Nature 2023 (2 papers), Cancer Discov 2022, ACIE, JACS, Mol Cell 2021, Nat Chem Biol, Nat Chem 2017, 2019, 2020, Nat Commun 2018, 2022, Science 2017). The discovery of a CD44-mediated iron endocytosis pathway that regulates cell state transitions in cancer and immune cells is remarkable. The team despite its modest size impressively succeeded in delivering interdisciplinary results, covering chemistry and biology expertise, in investing in innovation from patent filing (12 patents filed over the period) to biotech creation (Metal Therapeutics), in successfully training young researchers (6 PhD students over the period) as attested by their career path and in remaining connected to society at large through intense communication activities which include TV (TMC) and radio (France Inter, France Culture, Radio Classique) appearances and articles in national newspapers (Le Monde, le Journal du Dimanche,...).

Strengths and possibilities linked to the context

32 original articles were published since 2017, all of them in journals of high-visibility and outreach. Articles published as first/last or corresponding author(s) (18) demonstrate the remarkable expertise and originality of the team research (e.g. J. Am. Chem. Soc 2017&22, Angewandte Chemie 2017&22, Nature Chemistry 2017&2019). The team has taken advantage of collaborative work with internationally renowned scientific teams to apply its knowledge and knowhow for the development of targeted therapies (Science 2017, Nat. Chem. Biol. 2019, Nat Commun. 2018 & 2022, Oncogene 2022). Review articles (10, e.g. Nature Chem. Rev 2018, Molecular Cell 2022) and book chapters covering methodology (e.g. Methods in Molecular Biology 2021) complete the output.

6 PhD fellows and currently one postdoc were supervised. One team member has defended an HDR. Of note is the remarkable impact of the training within the team on the young researcher careers that obtained academic/industrial positions or pursued postdoctoral / doctoral training, in appealing international institutions. Researchers have joined the team during the period, as CRCN Inserm (2019) and CNRS (2021) or IR CNRS (2018) and Inst. Curie (2020).

The team has secured a very high level of funding in competitive calls at the European level (ERC consolidator grant) and national level (5 ANR and 3 Inca) or by charities (e.g. Ligue contre le cancer) and foundations (e.g. FRM).

International recognition of the group leader outstanding contribution to research and innovation is confirmed by numerous prizes that he received, in France (e.g. Prix Lacassagne from Collège de France, I-Lab award) and abroad (e.g. Fellow of the Royal Society of Chemistry). The team leader scientific recognition is also apparent in the very high number of seminars in renown international institutes (e.g. Cambridge University, Imperial college London) and conferences of the best scientific level (e.g. Keystone symposia, EMBL meeting). The team leader also contributed to scientific advisory board of several learned societies in France and abroad (e.g. Société de chimie thérapeutique), as well as charities (e.g. Ligue contre le cancer). The PI has shaped the field of chemical biology by contributing to journal edition (3 board memberships, 2 as editor), evaluation of manuscripts and by providing expertise to several national (e.g. ANR) and international (ERC) funding bodies.

The team has also outstandingly managed the impact of their fundamental research by filing seventeen patents on the period and creating two biotech companies, demonstrating its capacity for innovation. This maturation aspect of the team activities has been supported by several specific grants (CNRS pre-maturation, PSL maturation, SATT IdF Maturation).

The team has actively contributed to inform society at large through multiple interventions in media of quality: newspapers (e.g. Le Monde), radio-programmes (e.g. France Inter) and various events (e.g. Fête de la Science).

Weaknesses and risks linked to the context

No weaknesses were notified by the committee.

Analysis of the team's trajectory

A very strong foundation for new discoveries with high medical impact has been laid during this period, promising a stellar trajectory.

RECOMMENDATIONS TO THE TEAM

Keep up the outstanding work in fundamental science and continue to inspire and champion the chemical biology approach. Conserve the team dynamism and agility in the future larger configuration of the unit.

CONDUCT OF THE INTERVIEWS

Date

Start: 10 novembre 2023 à 08h30

End: 10 novembre 2023 à 17h30

Interview conducted: online

INTERVIEW SCHEDULE

CHIMIE ET BIOLOGIE DE LA CELLULE – November 10 2023

8:00 - 8:15 Testing Zoom connections

8:15 - 8:30 Closed session Expert Committee (EC) – Scientific Officer (SO)

Assessment of the Unit, Scientific Plenary session

8:30 - 8:40 Presentation of the EC to the staff members by SO

8:40 - 9:15 Presentation of the unit by Ludger Johannes (25 + 10 min questions)

Attending: EC, SO, all the unit members

Presentation of the teams

9:15 - 9:45 Chemical Biology – Raphaël Rodriguez

(15 min presentation + 10 min questions)

Attending: Team members, EC, SO, director of the Unit

+5' private discussion with the PI; attending: EC +SO

9:45 - 10:15 Membrane Mechanics and Dynamics of Intracellular Signaling – Christophe Lamaze

(15 min presentation + 10 min questions)

Attending: Team members, EC, SO, director of Unit

+5' private discussion with the PI; attending: EC +SO

10:15-10:45 Endocytic Trafficking and Intracellular Delivery – Ludger Johannes

(15 min presentation + 10 min questions)

Attending: Team members, EC, SO, director of Unit

+5' private discussion with the PI; attending: EC +SO

10:45-11:30 Break – Closed session with EC and SO

11:30-12:00 Closed session with researchers and professors

Attending: Researchers except group leaders, EC, SO

12:00-13:30 Lunch Break

13:30-14:00 Closed session with thesis students and postdocs

Attending: PhD students and postdocs, EC, SO

14:00-14:45 Closed session with technical and administrative personnel

Attending: Technicians, Engineers, Administrative staff, EC, SO

14:45-15:30 Break – Closed session with EC and SO

15:30–16:00 Closed session with the representatives of supervising bodies

Attending: expert committee, representatives of Institutions, SO

16:00–16:30 Closed session with the head of the unit

Attending: Unit Direction, expert committee, SO

16:30–17:30 Meeting of the Committee – Finalisation of the report (closed hearing)

PARTICULAR POINT TO BE MENTIONED

N/A

GENERAL OBSERVATIONS OF THE SUPERVISORS

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Objet

Comments to HCERES Evaluation report of the Unit
Cellular and Chemical Biology / CCB
DER- PUR250024515 - EV 0753172R
Evaluation campaign 2023-2024 / Group D

HCERES

For the attention of HCERES President,
Mr Stéphane Le Bouler
and the HCERES Expert Committee

Paris, 15th February 2024

Dear All,

We would like to start by thanking the chairman of the expert committee, Dr. Gilles Guichard, the HCERES representative, Dr. Marie José Stasia, and the members of the panel for their investment.

We were pleased to read that the unit and its teams were evaluated as outstanding, which is a strong encouragement for all unit members to pursue their exceptional investment in the unit's projects.

We have requested some changes in the report (please see the enclosed list), and in this letter you will find comments to some points raised in the report concerning globally the unit and specifically the Johannes team.

- On page 9 it is mentioned that *"The unit did not provide specific information on its position with regard to energy and resource saving, particularly in terms of travel management and waste treatment, for example"*. Even if these points were indeed not explicitly listed, they were summarized on page 10 of the Self-Assessment Document in the paragraph *"Compliance with health and safety regulations is a top priority for the Research Center as it contributes to the quality of life and working conditions of its staff"*. Indeed, the unit fully adheres to the sustainable development goals of the Research Center. This includes decarbonizing research activities, raising the awareness for sustainable development goals, providing training to integrate them into professional practices and projects, taking into account the "One Health" concept, and strengthening synergies with local stakeholders on these matters.
- The organic chemistry aspect is raised in the recommendations to the unit section on page 14: *"... addressing the current understaffing challenge in the administrative office is essential, as well as further enhancing chemistry expertise through the recruitment of new teams"*. Both aspects will indeed be addressed in the context of the project for the creation of the Chemical Biology of Cancer (CBC) unit, for which additional administrative personnel will be requested and the recruitment of 2 new chemical biology teams is programmed.
- *"Such publications could be detrimental to the decision of the ongoing evaluation of the ERC synergy grant"* (bottom of page 16). With all respect, we rather think that our high-profile stories will be appreciated by the ERC panel as the type of groundbreaking discovery that has the potential to be transformed by our proposed ERC program into a paradigm shift of general importance in the life sciences. We are optimistic that the ERC panel will recognize the quantum leap potential of our proposal.

- *“The maintenance and support of these novel technologies requires substantial funds that the team and collaborators must obtain in upcoming years”* (bottom of page 16). We would like to point out that an INSERM engineer position (IR) has been obtained and filled since January 17, 2024, for running the lattice light sheet microscope and for data processing. This constitutes an extremely solid and sustainable basis for the further development of this high-end instrument. In what concerns the mass spectrometry equipment for metabolomics and lipidomics, Institut Curie has hired Julio Sampaio (PhD) on a permanent contract basis to run the platform. After only 2 years of activity, he already generates a significant income from user fees and grants that he has obtained, which clearly documents the successful and sustainable implementation of the platform at Institut Curie and beyond (including European Union countries and the United States).

We trust that these comments will enlighten future readers of the HCERES report and convince them of the seriousness with which the recommendations of the expert committee are taken into account.

Yours Sincerely,



Pr Alain PUISIEUX
Directeur du Centre de Recherche de l'Institut Curie



Dr. Ludger JOHANNES
Directeur de UMR3666 / U1143

The Hcéres' evaluation reports are available online:
www.hceres.fr

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