Research evaluation

EVALUATION REPORT OF THE UNIT

IPMC - Institut de pharmacologie moléculaire et cellulaire

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Université Côte d'Azur - Uca, Centre national de la recherche scientifique - CNRS

EVALUATION CAMPAIGN 2022-2023

GROUP C

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In the name of the expert committee[1] :

Ludger Johannes, 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

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	Mr. Frederic Boccard, CNRS, Gif-sur-Yvette
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	Ms. Dominique Massotte, CNRS, Strasbourg
	Mr. Antonin Morillon, CNRS, Paris
	Mr. Laurent Venance, Inserm, Paris
	Mr. Lucas Jacques Waltzer, CNRS, Clermont-Ferrand

HCÉRES REPRESENTATIVE

Ms. Marie José Stasia
Mr. Yacine Graba

CHARACTERISATION OF THE UNIT

- Name: Institut de Pharmacologie Moléculaire et Cellulaire
- Acronym: IPMC
- Label and number: UMR 7275
- Number of teams: 20
- Composition of the executive team: Mr. Jean-Louis Nahon; Florian Lesage (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

Researchers at IPMC work on potential pharmacological targets, their functions in cells and their possible exploitation in biomedical research. Ion channels, membrane proteins and lipids, signalling factors, nucleic acids and their binding partners are key molecules that are investigated from several angles. The thematic areas that are addressed include neurobiological, immunological, functional genomics and membrane biological questions, and a wide range of pathological situations ranging from neurological disorders to cancer.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

IPMC was founded in 1989 by Michel Lazdunski who directed the until until 2003 when Pascal Barbry took over until 2017. In 2018, Jean-Louis Nahon became director. At its origins, IPMC was only affiliated with CNRS, which changed in 2000 when the local Nice Sophia Antipolis University also became an oversight body (Université Côte d'Azur since 2020). The institute is located in the Sophia Antipolis Technology Park in Valbonne in the south-east of France. The neighbourhood with a large hub for established and start-up companies provides an appropriate environment to foster the institute's ambitions of establishing ties with pharma and of creating biotech companies for the development of new therapeutic modalities. The institute has grown in size over the years from initially 4,700 m2 to 8,000 m2 today.

RESEARCH ENVIRONMENT OF THE UNIT

IPMC is embedded in the local, national, and international research environments. The link with the local Université Côte d'Azur (Uca) is materialised by five professors and associate professors and fourteen assistant professor positions. IPMC researchers are also strongly involved with the EUR-LIFE program at Uca, which structures training and research aspects of the life and health sciences. The EUR-LIFE program has the ambition to reach out for partner universities in other European countries. It houses thematic institutes such as Neuromod in which IPMC researchers are also involved.

IPMC is part of the excellence initiative (Idex) Jedi, under the leadership of Uca. The ambition is here to favour transdisciplinary training, research, and innovation programs.

IPMC was strongly involved with the laboratory of excellence (Labex) initiative. The Labex ICST on ion channels had a nationwide scope and was led by the current deputy director of IPMC. The Labex Distalz on Alzheimer's disease also had a nationwide scope. Discussions are currently ongoing as to mechanisms by which these Labex might continue to operate, possibly in alternative formats. The Labex Signalife on signalling pathways involved teams in the Nice area. It has now been restructured to support technology transfer projects.

Another regional initiative between Nice and Marseille in which IPMC is a driving force is the EquipEx 4D'omics. The goal is here to provide an integrated solution for acquisition, storage and analysis of omics data in 3D and time, also involving a link with the Interdisciplinary Institute of Artificial Intelligence 3IA-Côte d'Azur. In both cases, the leadership of a member of IPMC is recognised.

IPMC also houses other platforms that often have a regional, national, or even international dimension: Capabio (mass spectrometry for proteomics, lipidomics and metabolomics), GenomiX (ISO9001 certified), imaging and flow cytometry in the context of the regional Microscopy Imaging Côte d'Azur (Mica) platform (ISO9001 certified, and Cristal Collectif awards from CNRS for deploying the Omero database at the regional and national level), and a facility for an *in vivo* experimental models including a wide range of behaviour aspects. The first

three platforms are labelled by GIS (Groupement d'Intérêt Scientifique) Ibisa (Infrastructures en Biologie Sante et Agronomie).

IPMC favours technology transfer in partnership with CNRS Innovation, the Labex Signalife, and a number of private partners.

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

Permanent personnel in active employment	
Professors and associate professors	5
Lecturer and associate lecturer	14
Senior scientist (Directeur de recherche, DR) and associate	31
Scientist (Chargé de recherche, CR) and associate	32
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	45
Subtotal permanent personnel in active employment	127
Non-permanent teacher-researchers, researchers and associates	20
Non-permanent research supporting personnel (PAR)	28
Post-docs	0
PhD Students	43
Subtotal non-permanent personnel	91
Total	218

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

Employer	**EC**	**C**	**PAR**
CNRS	0	38	42
Inserm	0	25	0
Université Côte d'Azur	16	0	3
CHU Nice	2	0	0
Université de Cergy-Pontoise	1	0	0
Université de Technologie de Compiègne	0	0	0
inconnu	0	0	0
Institut Pasteur Paris	0	0	0
Total	19	63	45

UNIT BUDGET

Recurrent budget excluding wage bill allocated by parent institutions (total over 6 years)	9139.0
Own resources obtained from regional calls for projects (total over 6 years of sums obtained from AAP idex, i-site, CPER, territorial authorities, etc.)	3970.0
Own resources obtained from national calls for projects (total over 6 years of sums obtained on AAP ONR, PIA, ANR, FRM, INCa, etc.)	22,888.0
Own resources obtained from international call for projects (total over 6 years of sums obtained)	7329.0
Own resources issued from the valorisation, transfer and industrial collaboration (total over 6 years of sums obtained through contracts, patents, service activities, services, etc.)	4323.0
Total in K euros	47,649.0

GLOBAL ASSESSMENT

IPMC has a unique position in France in exploring pharmacology in many directions. Its research activities are outstandingly well funded (total budget of approx. €50 million). Unit members have been highly successful in obtaining regional (Uca, PIA, RHU…), national (ANR, INCa…), and international funding (ERC, Feder…). Notably ANR and EU funding has strongly increased in recent years. Most of the recurrent funding goes to the platforms, a policy that is embraced by the unit members. Part of the recurrent funding also goes into newly created transversal programs that have fostered internal collaborations (3% of the total budget). Recurrent funding is exceptionally used to support teams that are temporarily in financial difficulty, which speaks for a highly appreciated level of solidarity within IPMC. The replacement of five retiring team leaders from four teams by eight junior team leaders for six new teams testifies for the forward-looking staff policy at IPMC. IPMC appears extremely well managed for all aspects concerning human resources, safety, environment, and scientific assets. The unit director has created a culture of internal democracy that is highly appreciated at all levels.

Research at IPMC is globally excellent with outstanding international visibility in areas such as membrane biology, functional genomics, ion channels and neurobiology. The organisation of 70 national and international meetings by IPMC researchers and the invitation of IPMC researchers to speak at the most prestigious international meetings (Embo, Jacques Monod, Gordon…) bears witness to the attractiveness of the research that is performed within this unit. IPMC researchers are also invited to participate in national and international review bodies (e.g. Hugo, IUPS, IUPHAR, FRM…) and institutional steering committees (CoNRS, CSS Inserm…), which illustrates their outstanding scientific reputation. Via their membership in 'Horizon 2020' and 'Horizon Europe' EU consortia, IPMC researchers contribute to the construction of the European research landscape. IPMC platforms are of the highest international standards, which strongly contributes to the attractiveness of the unit. Mathematical modelling and computational developments are already present in several teams, involving in some instances co-supervised students. This illustrates a general capacity of the IPMC teams to adopt novel approaches to advance their projects. It also illustrates that IPMC provides highly attractive conditions for training young scientists, who are offered with an exceptional level of independence to get organized among themselves and to organise scientific events such as seminars and meetings.

The IPMC unit has published impactful and internationally visible scientific contributions in wide areas of research such as ion channels, neurobiology, functional genomics, and membrane biology (altogether 581 papers in the contractual period under review, with 126 of these papers in highest-ranking international journals with outstanding highlights, e.g. Cell, Nature, Nature Medicine, Immunity). The scientific production of the unit includes the training of students with 65 awarded PhD degrees in the contractual period under review, and 36 ongoing PhD projects. According to information that was available from the self-assessment document, researchers at IPMC generally comply with the principles of research integrity, ethics, and open science.

IPMC has the declared ambition to perform translational research and technology transfer. They have been outstandingly successful with this. Beyond patent filings (21 filings in the contractual period under review, of which 15 are under license), IPMC members have signed fifteen industrial contracts and created three start-up companies, with one more start-up company creation project that is currently ongoing. These socio-economic activities have generated more than 4 M€ of funding for IPMC. IPMC researchers have ties with physicians, e.g. from Centre Antoine Lacassagne, and Nice, Stockholm and Uppsala University Hospitals, to name a few. Discussions are currently ongoing with Université Côte d'Azur for the construction of a start-up company incubator, which would be a great additional catalyser for the technology transfer activities at IPMC. Teams at IPMC also heavily participate in outreach activities to the general public, e.g. seminars at local events, presence in print and online media, participation in open-science days, visits in schools, and interactions with patient associations (e.g. Association Vaincre la Mucoviscidose, France Alzheimer Côte d'Azur, France Cancer, Dravet syndrome organisations, Fondation Lejeune, Fondation Maladies Rares).

DETAILED EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The points that were raised in the previous HCÉRES report from July 18, 2017, have been well addressed. The improvements in response to the previous report have contributed to maintain IPMC as one of the most attractive research sites in France.

Strategy of future direction team and participation of team leaders in decisions:
Of foremost importance, the transition from the founding director of the actual one has been managed with success. Quite visibly, a high level of internal consultation and democracy has assured the adherence of unit members to the unit's project, smoothened unit life, and has allowed to organise the unit in an efficient manner. It also appears that the unit has mastered the Covid pandemic period without accidents and has kept a positive dynamic, despite the challenges that arose from the repeated confinement situations.

Need to attract external teams:
The contractual period under review has seen the arrival of three external team leaders. With two other teams that renew their current leaders by internal promotion based on an independent review procedure, both external dynamics and generational renewal have been instigated in the contractual period under review.

Attractiveness, including transversal axis, internal collaborations, and conference organisation:
The attractiveness aspect has been addressed by several actions, notably through the acquisition of new state-of-the-art equipment for the imaging, cytometry, metabolomics platforms, the introduction of transversal axes with dedicated funding, which has led to an increase of internal co-publications, the organisation of unit retreats in 2018 and 2022, the enhanced coverage of teams with at least one ITA, and the establishment of a grant program for students and postdocs for their participation in and organisation of international meetings.

Success for international/European grants:
The implication of the unit in international/European research funding schemes has been strengthened with the presence of IPMC researchers in several consortia. At the level of ERC, one synergy grant has been obtained. Very recently, an EIC grant was also secured. Six other team leaders have filed ERC proposals that progressed to variable levels.

B – EVALUATION AREAS

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

Assessment on the unit's resources

IPMC researchers have been exceptionally successful with competitive funding at regional, national and international levels. IPMC teams are thereby very well-funded (€50 million). One ERC synergy grant has been obtained and very recently one from EIC (European Innovation Council).
The recurrent funding at IPMC is to a large extent mutualised for platforms. In general, no recurrent funds go directly to the teams. This policy is largely supported by the team leaders.

Assessment on the scientific objectives of the unit

The main objectives of the unit are clearly outlined in accordance with these strengths, including measures to capitalise on these (e.g. transversal programs). New team leaders (external and internal) continue already existing lines of research or instigate entirely new orientations. The unit also has clear ambitions for technology transfer, including the creation of start-up companies.

Assessment on the functioning of the unit

After having been elected in 2018 by the unit members of IPMC, the Director has succeeded in keeping everyone on board. A team leader council was put in place that meets once a month with the unit director to discuss all matters pertinent to unit strategy. This exemplary level of internal democracy is largely perceived very positively. The strong position of the platforms in the research landscape of IPMC is another defining element, which equally is positively perceived. Overall, the unit appears to be fully functional to pursue its ambitious objectives.

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

Strengths and possibilities linked to the context

The unit has a total budget of approx. €50 million for the contractual period under review. The recurrent funding represents 19% of this budget.

Recurrent unit resources are used to subsidise IPMC's platforms which clearly represent an outstanding strength of the institute. The success with competitive funding (e.g. European funding via the Sables project, national funding via Itmo, regional funding via Paca…) assures that the platform equipment is maintained up to date.

Part of the recurrent funding also goes into a newly created transversal program that is geared as fostering internal collaborations. Recurrent funding is exceptionally also used to support teams that are temporarily in financial difficulty.

Unit members are successful in obtaining regional (from Uca, PIA such as Labex, Idex, EquipEx…), national (notably 56 ANR grants of which 33 are coordinated by IPMC researchers…), and international funding (EU, 6 of these exceeding 500 k€ each…) and one ERC. The success with ANR and EU funding has strongly increased in recent years. The institute's teams overall appear to have the required resources to pursue their mission in excellent conditions. This includes funding for start-up companies from regional (Signalife…), national (CNRS Innovation…) and private sources.

Weaknesses and risks linked to the context

The unit is very well funded. No obvious weakness or risk at this level.

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

Strengths and possibilities linked to the context

IPMC has a unique position in France in exploring pharmacology in many directions, including the neuroscience, endocrinology, immunology, behavioural aspects, membrane biology, signalling, epigenetics and genomics.

The leaders of teams n° 5, n° 8, n° 10 and n° 20 will leave their management responsibilities. Their replacement was a critical aspect. Eight new junior team leaders were recruited by internal promotion or from the outside of IPMC through an independent review procedure involving the external advisory committee in addition to the team leader council.

The platforms are another strength on which IPMC researchers can capitalise in the pursuit of their scientific objectives. The modernisation of platform equipment is a critical asset that was achieved based on success with competitive funding applications. Forward-looking strategic planning also concerns projects for new platforms in bioinformatics and genome editing via CRISPR-Cas9.

Weaknesses and risks linked to the context

One aspect that might be worth considering in terms of forward-looking policy is thematic renewal or intensification outside areas that are currently already strongly covered at IPMC. Computational biology is one of these with which the platform project on bioinformatics might be affiliated. Such development would be

expected to strongly benefit not only omics approaches that rely on statistical methods, but also the understanding of biological structures with potentially druggable sites on proteins, and complex biological processes with emerging properties based on weak interactions.

Structural biology might also be an area that could benefit from additional strategic planning. With the 'resolution revolution' in cryo-EM/ET, structural biology has become even more centre stage in the life sciences as before by allowing addressing difficult objects (such as membrane proteins) more 'easily' and within their natural context. Several teams at IPMC collaborate already with structural biologists for cell biology or molecular pharmacology projects. It might be of strategic importance to consider possibilities for optimising the conditions under which research within the unit could benefit ever more from this game changing progress in the life sciences.

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

IPMC appears extremely well managed for all aspects concerning human resources, safety, environment, and scientific assets. The unit director is widely recognised for his devotion to dealing with problems, including notably also human resource problems, in a constructive manner. He has created a culture of internal democracy that is appreciated at all levels. With the help of the regional delegation of CNRS, this competent management has allowed to handle the two major crises of the contractual period under review: persistent cases of contamination in the IPMC II building that were solved only when all ventilation tubings were fully cleaned, and the COVID pandemics. From the detailed self-assessment document and the discussions on site it clearly appears that personal health, well-being, and safety of the unit members are well looked after.

The unit's level of gender equality is higher than the average of the CNRS Life Science institute INSB. Substantial efforts have been made to encourage the promotion of technicians and engineers of the unit. Training through research was facilitated by a travel grant program that has been amplified.

A sustainable development referent was appointed in 2020, and several actions have been taken (recycling, reduced carbon footprint…) to take the environmental impact into account.

Scientific assets are protected in dedicated data storage facilities. These are extended based on funding that was obtained in different types of calls (EquipEx 4D-omics, Molecularxiv, Oligoarchive…). Scientific assets are also protected by patent filings, which are handled by a member of IMPC with the help of the regional delegation of CNRS, CNRS Innovation, the SATT Sud-Est, etc.

Weaknesses and risks linked to the context

As noticed by the unit director himself in the self-evaluation document, women are underrepresented in IR and DR positions. This is more generally also the case in the life science institute of CNRS. This imbalance might be counteracted in future rounds of recruitment and promotion if correspondingly qualified women researchers have applied.

The creation of an ethics committee and the nomination of a designated mediator for confidential matters related to possible situations of conflict would appear as recommendable measures for optimal management of psychosocial risks.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

Research at IPMC has outstanding international visibility in several fields such as membrane biology, functional genomics, ion channels and neurobiology. IPMC provides highly attractive conditions for research because of inclusive and democratic leadership, competitive platforms, an environment of outstanding teams and team leaders, excellent funding conditions, a dynamic integration within the scientific landscape at Uca and south-eastern France providing access to students and complementary expertise, and a beautiful setting within one of the most scenic parts of France.

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

Strengths and possibilities linked to the context

The organisation of 70 national and international meetings by IPMC researchers and the invitation of IPMC researchers to speak at the most prestigious international meetings (Embo, Jacques Monod, Gordon…) bear witness to the attractiveness of the research that is performed at the institute. IPMC researchers are also invited to participate in national and international review bodies (e.g. Hugo, IUPS, IUPHAR, FRM…) and institutional steering committees (CoNRS, CSS Inserm…), which illustrates their scientific reputation. Via their membership in 'Horizon 2020' and 'Horizon Europe' EU consortia, IPMC researchers contribute to the construction of the European research landscape.

Weaknesses and risks linked to the context

No obvious weakness or risk.

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

Strengths and possibilities linked to the context

In the contractual period under review, IPMC has attracted external and internal junior scientists for the leadership renewal at the head of existing teams and created one new team.

Furthermore, nine researchers newly joined the unit, who obviously reinforce IPMC in general in a decisive manner, and in particular, naturally, also the corresponding teams. All these documents show that the unit is attractive also to young researchers and provides a favourable environment for the development of their careers. 21 unit members have received prices, including CNRS medals. Access to platforms, administrative help, clear bylaws with commitment to research integrity and open science add to the attractiveness profile of IPMC.

Weaknesses and risks linked to the context

It appears striking that none of the junior team leaders at IPMC holds prestigious starting or consolidator ERC grants. The unit may explore schemes that would encourage corresponding applications and/or optimise their chances of success. Furthermore, the apparent difficulty with attracting top-level external mid-term career stage team leaders with corresponding funding may also be addressed. This would further help to further sharpen the international visibility of IPMC.

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

IPMC researchers are highly successful with regional, national (notably 56 ANR grants of which 33 are coordinated by IPMC researchers), and international grant applications (6 of these exceeding 500 k€ each, such as ERC synergy, Feder, ONO Pharma). Of note, IPMC researchers have obtained substantial funding

through the Programme d'Investissement d'Avenir (PIA), i.e. through the EquipEx (1), Labex (3) and Idex (1) instruments. At the level of ERC, one synergy grant has been obtained during *the* contractual period under review, and six other proposals have been filed that progressed to various levels. During discussions on site, the very recent success with a European Innovation Council (EIC) grant and the possible recruitment of an external team with an ERC grant were mentioned by the unit director.

Weaknesses and risks linked to the context

No obvious weakness or risk.

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

Strengths and possibilities linked to the context

The recurrent budget at IPMC is largely invested to subsidise the institute's platforms. The reward for this is that these platforms are of the highest international standards. Notably the functional genomics, imaging, and mass spectrometry platforms have received the GIS (Groupement d'Intérêt Scientifique) Ibisa (Infrastrutures en Biologie Santé et Agronomie) label. The facilities for in vivo experimental models Anipro and Animex have undergone a complete resetting (point zero) during the contractual period under review. The Animex facility allows addressing complex behavioural aspects.

IPMC has put in place an ambitious strategy for the maintenance and renewal of platform equipment for which competitive funding has been obtained in the contractual period under review. The platforms are open not only regionally within the academic perimeter of Uca, but also to other academic institutions and companies (e.g. E-Phy-Science, Sangamo, Inrae, Coraliotech, CEPAM, C3M, Ircan, ICN, Institut Jacques Monod, Institut Pasteur de Lille).

Mathematical modelling and computational developments are already present in several teams, involving in some instances co-supervised students under the 3IA-Côte d'Azur institute umbrella, showing the capacity of the IPMC teams to adopt novel approaches to advance their projects, e.g. software development for image analysis, bioinformatics suites to analyse omics, mathematical models of tumour-immune system interactions. Some of these tools have been made open access and available to the community on GitHub.

Weaknesses and risks linked to the context

One of the possible risks with the platform situation at IPMC is that recurrent funding is entirely devoted to their maintenance and development such that none of these funds reaches the teams directly. It is therefore key to ascertain the continued adhesion of IPMC researchers with this strategy. For this, it will be instrumental to maintain the platforms at highest possible international levels and of widest general interest such that – as a whole – they render service to each and every team at the institute. It will also be of strategic importance to plan on the extension of the scope of platform activity, as it is already mentioned in the self-assessment document and reiterated during the site visit for bioinformatics and genome editing. In consideration of requested funds, such planning may in some cases need to be done at the level of Uca and/or the south-eastern France area (e.g., for strengthening the structural biology aspect of IPMC research). In as much space allows this, the scope of the Anipro and Animex facility might be reviewed to include different species. For a pharmacology unit this would be an advantage for the testing of drug candidates in accordance with the 3R rules on this kind of research.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

IPMC is internationally at the forefront of science in dynamic areas such as ion channels, neurobiology, functional genomics, and membrane biology, to name a few. This has led to the publication of 581 papers in the contractual period under review. 126 of these papers were published in highest-ranking international journals with outstanding highlights. This exceptional scientific output is shared between most teams at IPMC.

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

Strengths and possibilities linked to the context

The historical focus of IPMC on molecular pharmacology, ion channels, electrophysiology, and protein biochemistry is still visible today and has been extended to neuroscience, cell biology, functional genomics, and physiology along four transversal scientific axes. Molecular pharmacology remains the unifying theme, and the 581 publications in the contractual period under review are distributed across all domains of research at IPMC. Of these 581 publications, 126 have come out in highest-ranking international journals from Springer-Nature, Cell Press, Science/AAAS … publishing groups.

The scientific production of the unit includes the training of students with 65 awarded PhD degrees in the contractual period under review, and 36 ongoing PhD projects.

Weaknesses and risks linked to the context

The obvious attractiveness of IPMC to a large extent depends on its documented success with publishing papers in journals whose international visibility is generally considered to be outstanding. The standards for this are often the use of a wide breadth of interdisciplinary techniques, e.g. physiological models or structural approaches. IPMC is providing excellent conditions for that with platforms that are of the highest international standards. Maintaining this level of competitiveness will be key for keeping IMPC researchers at the forefront in science. Building stories that can compete for space in top-tier journals most often also needs time, and internal funding (e.g. from the transversal axes budgets) might sometimes help to support teams during lengthy revision processes. Any of these measures might be considered to support IPMC researchers in their continued quest for outstandingly impactful research.

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

Globally at the unit level, the scientific production is truly exceptional for a unit with 20 teams and 4 major platforms.

Weaknesses and risks linked to the context

The scientific production is proportionate to the research potential of the unit. No obvious weakness or risk can be detected.

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

According to information that was available from the self-assessment document, researchers at IPMC generally comply with the principles of research integrity, ethics and open science.

Weaknesses and risks linked to the context

In the discussions on site, it was mentioned by the unit director that an ethics committee will be put in place, which was perceived as a highly recommendable course of action. The nomination of an officially appointed mediator would also appear highly recommendable.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

IPMC has the declared ambition to perform translational research and technology transfer. Beyond patent filings (21 filings in the contractual period under review, 15 under license), IPMC members have signed fifteen industrial contracts and created three start-up companies, with one more creation project that is currently ongoing. These outstandingly successful socio-economic activities have generated more than four million Euros of funding for IPMC. IPMC researchers have ties with physicians, e.g. from Centre Antoine Lacassagne, Nice, Stockholm and Uppsala University Hospitals, to name a few.

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

Strengths and possibilities linked to the context

IPMC researchers develop documented activities for technology transfer and reach-out to the general public. Both the volume and quality of these activities appear highly appropriate with respect to the size of the unit. A lecturer/hospital practitioner (MCU-PH Uca) has joined the IPMC to strengthen four research teams,

Weaknesses and risks linked to the context

No obvious weakness or risk.

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

Strengths and possibilities linked to the context

The scientific activities at IPMC generate scientific knowledge and technological know-how that has outstanding potential for the development of marketable products. IPMC researchers get personally involved through patent filings, industrial collaborations, and start-up company creations. They are supported for this by an internal personnel whose work is dedicated to accompany technology transfer activities, often in relation with Uca (via the Labex Signalife), and nationally with CNRS Innovation. Other than generating resources for IPMC, these activities also sustain employment in the region. IPMC researchers also have ties with physicians, e.g. from Centre Antoine Lacassagne, Nice, Stockholm and Uppsala University Hospitals, to name a few, and they have been involved in clinical trials, e.g. fragile X syndrome patients in a Phase II clinical trial, schizophrenia patients in several trials, adrenocortical tumours in children, evaluation of the therapeutic potential of Varespladib to treat Covid-19 patients.

Weaknesses and risks linked to the context

By liaising with regional (Uca Labex Signalife) and national partners (CNRS Innovation), IPMC has been highly successful with fostering its technology transfer ambitions. During the site visit, the unit director mentioned that the laboratory space at IPMC is not sufficient to incubate start-up projects internally. Alternative solutions should be pushed with vigour. One of these is the BioIncubSophia initiative with Uca.

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

Strengths and possibilities linked to the context

Teams at IPMC participate in outreach activities to the general public. These include seminars at local events, presence in print and online media (including science movies), participation in open-science days (Fête de la Science, Pint of Science…), visits in schools to talk science to the youngest (Cordées de la Réussite…), and patient associations (e.g., Association Vaincre la Mucoviscidose, France Alzheimer Côte d'Azur, France Cancer, Dravet syndrome organisations, Fondation Lejeune, Fondation Maladies Rares).

Weaknesses and risks linked to the context

No obvious weakness or risk.

C – RECOMMENDATIONS TO THE UNIT

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

Make sure that the harmonious and productive way of unit organisation at IPMC is handed over to future directors. Possible optimisations: Presence of platform managers as observers during the team leader meetings, diffusion of the team leader meeting reports to unit members.

Option to reinforce scientific axes: Internal seminars according to the axis to further strengthen the interactions between unit members.

Maintain competitiveness (e.g. renewal of instruments, new models), accessibility, and dynamics (possibility to open new platforms in function of emerging scientific needs) of platforms.

Capitalise on the opportunity of future recruitment to reinforce strategic area of research, according to the 'contained, without missing any opportunity' scheme that is mentioned in the self-assessment document.

Clearly identify the principal investigators for each project (project leaders) in each team, e.g. on the internet page of the unit. This will notably increase the visibility of young scientists in well-established teams.

The creation of an ethics committee and nomination of a designated mediator for confidential matters related to possible situations of conflict would also appear recommendable.

Optimise procedures that are pertinent to ecological matters ('Green Lab').

Best efforts should be made to propose as much alternative lunch options as possible to IPMC researchers by respecting their wish to be able to have lunch together independently of their employment situation.

Recommendations regarding the Evaluation Area 2: Attractiveness

The continued attractiveness and international visibility of IPMC depend on many of the points that are listed above. IPMC's imbrication with the regional scientific tissue at Uca also is of critical importance in this context for access to well-trained students (PhD program), funding (Programme d'Investissement d'Avenir), and additional interdisciplinary expertise, e.g. chemistry, physics, mathematics, informatics. IPMC researchers are already driving forces at several levels of the interface with Uca, which should be maintained and if possible extended (e.g. opportunities to reinforce strategic areas of research).

Several of the externally recruited or internally appointed new team leaders will continue the activity of existing teams. Care should be taken to assure that also in these cases, thematic reinforcement and/or renewal will be assured in areas that might be of strategic importance to IPMC.

Recommendations regarding Evaluation Area 3: Scientific Production

The scientific production at IPMC is truly excellent with outstanding highlights (e.g. the human developmental cell atlas, functions of the non-coding genome, entropic barriers to control protein dynamics on membranes,

links between neuronal/brain functions and immunity, mechanisms of ion channel activity and behaviour). The use of prepublication repositories like bioRxiv might be further intensified by researchers at IPMC as part of a worldwide move towards open science. Articles that are deposited in such repositories are increasingly used for decision-making on fellowship and grant applications.

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

Researchers at IPMC are strongly involved with nonacademic interactions, notably for technology transfer to the socio-economic world. To optimise these efforts, additional lab space for early-stage start-up company incubation would be needed. Opportunities such as the BioIncubSophia initiative with Uca should be pursued with determination.

TEAM-BY-TEAM ASSESSMENT

Team 1: Dynamics of lipid membranes and protein coats

Name of the supervisor: Dr Bruno Antonny

THEMES OF THE TEAM

The team has fundamental interests in membrane dynamics, in the link between polyunsaturated lipids and membrane mechanical properties, in signalling by membrane curvature and in transport of lipids at membrane contact sites. The team contributed to the understanding of membrane structure and function, by studying the lipid transporter OSBP that use cellular PI4P to exchange cholesterol. OSBP is a pharmacological target of interest explored in a collaborative medicinal chemistry project. The team has also investigated the roles of intrinsically disordered regions of proteins to facilitate their diffusion into membranes. The role of acyl chain asymmetry and poly-unsaturation of phospholipids in membrane vesiculation is another original contribution to knowledge.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

· The relative lack of translational aspects could be a criticism addressed at this group.
The team participated to a collective research effort on Sars-Cov2 to verify interactions with potential cellular partners of each individual virus protein. The corresponding article has been published in Biology of the Cell (Miserey et al 2021).
Compared to the previous reporting period, the team has been more active in translational research through national collaborative work and supported by a SATT project (Paris-Saclay), which led to two patents.
Most importantly, a large EU H2020 funding (Spheres) under the Synergy ERC project scheme will shape the team project in the next few years (2020-26). This Spheres project has direct link to several pathologies, including cardiometabolic diseases.

· The group should consider expanding, particularly the number of PhD students (3 in the previous period) but this is more of a suggestion than a recommendation.
This recommendation/suggestion has been followed given that three PhD students have defended their thesis and two third-year PhDs are ongoing. Notably, four habilitations (HDR) have been obtained in the team, providing a striking increase in the supervision potential.

· The team should expand to fill the gap left by the departure of Drin.
No recruitment has happened during the period but the supervision potential has increased

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	3
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	0
Subtotal permanent personnel in active employment	**5**
Non-permanent teacher-researchers, researchers and associates	1
Non-permanent research supporting personnel (PAR)	3
Post-docs	0
PhD Students	2
Subtotal non-permanent personnel	**6**
Total	**11**

EVALUATION

Overall assessment of the team

The team is highly focused on fundamental research questions addressed by an interdisciplinary approach to decipher mechanisms at the molecular and cellular scales, including in silico approaches and 3D cell cultures. The team had an excellent to outstanding research production and contribution to knowledge during the period. The originality and importance of their research lead to their successful application to an H2020 Synergy ERC grant showing the outstanding attractiveness of the team research. Team members had an excellent supervision activity and four HDR were defended during the period.

Strengths and possibilities linked to the context

Team members combine expertise in biochemistry, cell biology and molecular dynamics simulations to study membrane biology mechanisms and to develop new original models.

Team members have published 31 articles with eighteen research papers, including ten as main authors and thirteen reviews. Research articles are published in very high quality journals such as Embo J, eLife, Dev Cell, J Cell Sci, Nature Com., J Biol Chem, J Mol Biol, and biology of the Cell. Reviews are published in excellent journals such as Ann. Rev. in Biochem. Publications as main authors in Soft matter journal (2020) and Biophysical journal (software PackMem, 2018) confirm the interdisciplinary capacity of the team. Team members acted as editors for several journals, contributing to shape the field.
The team has been very successful at funding its project at the regional level with two contracts and within the PIA Signalife initiative. In addition, team members coordinated two ANR projects and joined a third one as partner. The team also received an 'FRM team' funding (2018-2021). Notably, at the European level, a Synergy ERC collaborative project (Spheres) will shape the team project in the next few years (2020-26). The Spheres project has a translational aspect as the studied adipocyte hypertrophy due to larger than normal lipid droplets, has direct link to cardiometabolic diseases.
Team members have received several prices: 2 'Prix d'excellence de l'Université Côte d'Azur', Journal of Lipid Research Junior Investigator Award and EBSA Avanti prize. Team leader gave a Keynote speech at the Gordon

research conference on Molecular and Cellular Biology of Lipids (USA). Principal investigators were invited to multiple international conferences or workshops (e.g. Embo workshops on membrane fission, 2016 and on lipid function in health and disease, 2019), contributing to the team outstanding project visibility. Team members contributed to the organisation of conferences (e.g. congrès 'building the cell', 'imaging the cell' …). Team members have provided recommendations on behalf of multiple supervising and funding bodies Hcéres, ANR, CSS1, CoNRS22, selection committee of Advanced ERC.

Team members have supervised five PhD students during the period including two ongoing third-year PhDs. Notably, four habilitations (HDR) have been obtained, providing a striking increase in the supervision potential. In addition, the results from the PhD students in terms of publications are excellent, showing that the supervision is of high quality. Two postdoc fellows have also joined the team during the period and published their research results as first authors.

The team has received one funding by the Foundation NRJ/Institut de France and funding for a fourth-year PhD fellowship from the FRM. The team has published two articles for a broader public in the journal Médecine/Science. Team members are co-inventors on two patents covering new compounds with therapeutic potential that target the activity of OBSP.

Weaknesses and risks linked to the context

The lack of general public involvement could be a weakness.

RECOMMENDATIONS TO THE TEAM

- Take the opportunity of the Spheres synergy grant to increase communication to the general public.

- Maintain outstanding fundamental mechanistic research and multidisciplinary expertise.

Team 2: Physiological genomics of the eukaryotes

Name of the supervisor: Dr Pascal Barbry

THEMES OF THE TEAM

The team is interested in RNA biology with a particular focus on human lung epithelial cells.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous committee suggested that the team should integrate additional types of data (i.e. epigenetic changes) and to use more in vivo approaches/data.
The team has used human biopsies to establish the transcriptional profile of the airways at single cell resolution but the integration of epigenetic or in vivo experimental setup was not implemented yet.

It was mentioned that the team should increase its implication/recognition at the European and international level and secure more funding.
These recommendations have been taken into consideration. The team is involved in a European H2020 consortium, contributes to the Human Cell Atlas international network, and the PI is clearly recognised at the international level. The level of funding of the team during the contract was very high.

It was indicated that the team should increase its translational activity.
While the team contributed to Covid-19 surveillance in wastewater and developed new technologies, it did not substantially increase its interactions with the hospital or its valorisation activities.

It was recommended to improve the organisation of the team and considered that the emergence of a new team within the same institute was not the most appropriate.
The team was reorganised: two researchers left the team (and set up a new team in the institute in 2017), one associate professor (MCU) was recruited in 2019.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	2
Senior scientist (Directeur de recherche, DR) and associate	3
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	**8**
Non-permanent teacher-researchers, researchers and associates	2
Non-permanent research supporting personnel (PAR)	1
Post-docs	0
PhD Students	2
Subtotal non-permanent personnel	**5**
Total	**13**

EVALUATION

Overall assessment of the team

The team develops cutting edge research and its level of production is outstanding, with some remarkable publications (Nature Com, Nature Med, NAR…). Its attractiveness is outstanding too: the team benefits from a very strong international recognition and obtained important funding support at the national and international level (FRM, ANR, H2020…). Its socio-economic contributions are very good.

Strengths and possibilities linked to the context

This very well-established team pursues original and relevant lines of research. It made several important discoveries during the evaluated period and remained at the forefront of scientific research thanks to the use and development of cutting-edge technologies: ribosome profiling, Scrna-seq, long-read sequencing, 3D culture, human biopsies… Its expertise in human airway epithelium and NGS were instrumental to reveal some aspects of Sars CoV-2 infection. New approaches combining 10X microfluidics or 10x Visium transcriptomics with 3rd generation sequencing (Nanopore) and bioinformatics to investigate RNA splicing events with single-cell or spatial resolution. The team published nineteen research articles as chief author mostly in highly-regarded journals (Am J Respir Crit Care Med, Circulation, Development, 3 Nat Comm, 2 Nat Med, Nucl Acids Res, PLoS Genet…). 25 articles in collaboration (e.g.: Cell, Cell Metab. Cell Syst, Elife, Nature…) and seven reviews.
The international reputation of the team is clearly attested by fruitful high-impact collaborations, more than 40 oral presentations at conferences (including Gordon/Faseb, American/European cystic fibrosis associations, France Génomique…). The team leader was awarded a knighthood from the Legion d'Honneur and a local price. He is involved in various scientific bodies (GIP Cancéropole Sud Ouest, Idex Jedi, CHU Nice, Vaincre la Mucovisidose, Uca GenomiX, France Génomique, International Human Cell Atlas Lung/Dev Biol – Inserm Cross cutting program). Strong implication in the Uca GenomiX platform and more recently of the Equipex 4 D-Omics for quantitative multi-scale biology.
The team obtained consequent fundings from competitive calls (around 4M€ during the period) at the national (1FRM Team, 1 INCa + 1 ANR as coordinator, 3 ANR as partner) and international levels (e.g. H2020 consortium DiscovAir, 2 grants from the Chan-Zuckerberg foundation). It also benefited from regional supports, notably through PIA initiatives (EQUIPEX 4D-Omics, Labex Signalife).
Recruitment of one Maitre de Conférence with competences in bioinformatics in 2019, one postdoc and eight PhD students (2 ongoing). One team member was promoted from CR to DR, one DR and one CR (both with HDR) left the team in 2017 to create a new team in the institute (Team 17).
The bioinformatics pipelines developed by the team (with team 23) were made available on Github or Bioconductor. Almost all the publications are in open access.
The team contributed to health surveillance policies during the Covid-19 outbreak thanks to the development of sensitive & cost-effective methods to detect Sars CoV-2 variants in waste waters, which led to contracts with Nice Metropole and Veolia. It has also established links with biotech companies (10X Genomics, Oxford Nanopore) to develop new sequencing strategies and it is associated with the FHU OncoAge. Some members of the team are present in social media (Linkedin, twitter) and have appeared in movies (journal of the CNRS, communication of Veolia).

Weaknesses and risks linked to the context

The departure of two researchers with HDR has reduced the operating/supervising capacity of the team. Two more researcher are expected to leave the team soon (retirement).
The microRNA axis of the team appears weaker than the other thematic.
While the team has made important technological advances, it did not file any license and its interaction with biotech companies does not seem to have been formalised.

RECOMMENDATIONS TO THE TEAM

- The team should increase its recruitment of postdocs and PhD, notably at the international level.

- All the researchers/MCU of the team are strongly encouraged to apply for an HDR.

- The projects seem strongly technologically-driven and more emphasis could be put on the underlying biological questions.
- The distinction between the activities of the team and that of the GenomiX platform should be clarified.

- Even though it shouldn't be its main objective, the team has the potential to increase its valorisation activity and to develop translational lines of research.

- The future of the team should be planned well in advance.

Team 3: RNA metabolism and neurodevelopmental disorders

Name of the supervisor: Dr Barbara Bardoni

THEMES OF THE TEAM

Team 3 studies Developmental brain disorders (DBD) with a focus on the Fragile X Syndrome (FXS), caused by the silencing of FMR1 and loss of the RNA-binding protein FMRP. During the last six years, the team aimed to better understand the molecular and pathophysiology of FXS and other DBD to define potential therapeutic strategies. They developed cellular models (shFmr1 in mES) and in vivo models. In addition, screens targeting FMRP interacting proteins, modifications or associated mRNAs revealed a critical role for FMRP sumoylation, defined five new RNA-binding motifs and revealed Pde2a mRNA and Cav2 as repressed targets. Phamacological inhibitions of Phosphodiesterase2a and other factors are important strategies now to develop translational and therapeutic approaches for FXS.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Increase the workforce or restrict the project to fewer direction
While the workforce did not increase, the projects are well oriented with numerous collaborations.

The only recommendation would be to advertise postdoctoral offers in a more international way to attract foreign postdoctoral fellows.
Not addressed, but two French postdocs during the last six years.

In regard of the field of research, more transfer activity should be given priority in the coming years, (..). Attempts should be made to bring forward recent discoveries of the team such as FXS treatment. This aspect is currently absent of the team activity.
This recommendation has been addressed with a patent delivered for a therapeutical treatment.

Technical assistance is needed in the team, and the team needs to be increased in size given the proposed project. The committee of experts is very much in favour of the arrival of new staff scientist, a permanent researcher who will bring the Drosophila model to the laboratory.
The Drosophila model has been brought to the lab but no permanent position yet.

The team might want to dedicate more time to training (more than 10%) from now on, as the number of HDRs will double.
The team has taught four PhD during the period but the number of HDR did not increase.

The team would benefit from a consolidation of financial support, especially to hire international postdocs. The main recommendation is to adapt the research plan to the workforce, (..).
Not addressed.

WORKFORCE OF THE TEAM

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

EVALUATION

Overall assessment of the team

The scientific production is excellent to outstanding given the size of the team with 40 publications (29 original, 10 reviews, including sixteen as leader; Stem Cells, 2017; NAR 2018; Genome Res, 2020). The visibility of the team is excellent to outstanding judged from successful fund-raising (1800kE, 2 ANR, 1 FRM, 1 MSCA, 1 Horizon, 3 awards), several meeting organisations (2nd Trisomy 21 Conference). Team members are members of scientific societies and journals' editorials (Neuroscience…). The non-academic activities are excellent with one patent and contacts to grand public (autism families).

Strengths and possibilities linked to the context

The scientific production of team is excellent to outstanding given the size of the team with 29 original articles, ten reviews and one patent. Ten original as last or corresponding author (Stem Cells, 2017; Dis Model Mech, 2017; Nucleic Acids Res, 2018; Front Mol Biosci, 2018; Cerebral Cortex, 2019; Mol Therapy Nucleic Acids, 2019; Front Mol Neurosci, 2018; Genome Res, 2020; Front Genet, 2021; Am J Med Genet, 2021); Six reviews as corresponding authors (Neurogenesis, 2017; Front Mol Neurosci, 2018; Mol Psychiatry, 2021; Front Mol Neurosci 2021).
The visibility of the team is outstanding with excellent raising capacities with up to1800kE within six years (2 ANR, 1 FRM, 1 MSCA, 1 Horizon and several national and international foundation fundings). The team is extremely well recognised with two awards during the period (Prix « Valérie Chamaillard », Prix Jeune Chercheur). They organised several meetings nationally and internationally (The multiple facets of RNA, Nice, 2018; Workshop' ERI-W, Helsinki, 2019; 2nd Trisomy 21 Research Society International Conference, 2017; Scientific Board of the 11th SifrARN, 2018; XIX Workshop Fragile X, 2019). They also are members of societies (Society for Neuroscience; Trisomy 21 Research Society; Federation of European Neuroscience Societies) and members of editorial board for journals (Plos One, Frontiers in RNA Networks and Biology; Frontiers in Molecular Neuroscience; Frontiers in Genetics Frontiers).
The non-academic activities of the team are excellent to outstanding given the size of the team with one patent in progress, participation to Pitch Accelerate, Innov'in Med (Marseille, France). The tam also participated to

annual meetings with families and patients affected by intellectual disabilities, to the writing of theater piece (Festival d'Avignon, July 2018), to 'The intellectual disability' Brain awareness weeks, and they are present on social networks and broadcast ('La Méthode scientifique' France Culture).

Weaknesses and risks linked to the context

No weakness identified except the low critical mass for permanent scientists, that could put the team at risks for development and continuation of projects.

RECOMMENDATIONS TO THE TEAM

The team has an excellent to outstanding production within a very competitive environment. Identification and promotion of future recruitment are important for future developments.

Team 4: Immune regulations at mucocutaneous surfaces

Names of the supervisors: Dr Véronique Braud and Fabienne Anjuère

THEMES OF THE TEAM

The team is focusing on the interplay between immune cells and non-immune components that takes place in epithelial tissues during the progression of cutaneous and mucosal head and neck squamous cell carcinoma. Using preclinical models and human biopsies, it combines fundamental and translational research aimed at understanding epithelial tumour development and providing new targets for cancer prevention and treatments.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous committee recommended that the team (1) increases its publication output, (2) further merges the projects of the two team leaders, (3) increases its international visibility, (4) consolidates its industrial collaborations, (5) sharpens its focus, (6) expands the teaching activities.

Points 2, 4 and 5 have been well considered as the team develops more synergistic lines of research that benefit from the two PIs' expertise and has substantial links with the industry.

Points 1, 3 and 6 were not addressed.

WORKFORCE OF THE TEAM

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

EVALUATION

Overall assessment of the team

The team develops original lines of research and has a very good to excellent production given its size. Its attractiveness is excellent: it is very well funded and attractive for PhD and postdocs albeit two PhD left the team without no first author publication. Its socio-economic interactions are excellent to outstanding, with a very strong valorisation activity.

Strengths and possibilities linked to the context

This small team developed a sound line of research on epithelial tumour progression in both in vivo preclinical models and human biopsies. It makes use of a strong combination of techniques, including transcriptomics, flow cytometry, mass cytometry, imaging, bioinformatics and mathematical modelling. It has produced some interesting results in onco-immunology, in particular concerning the mechanisms of immune suppression associated with aggressive cutaneous and mucosal head and neck squamous cell carcinomas (HNSCC). The team also developed new valuable protocols for mass cytometry imaging and cytotoxic assays. Team members published nine research articles in speciality journal of the field (1 Cancers, 2 Frontiers Immunol, 2 J Invest Dermatol, OncoImmunol, PLoS One…) as main authors, including three method-oriented papers. They also contributed to one review and four collaborative research articles.

The team attracted five PhD students (2 ongoing) as well as three postdoctoral fellows. One of them set up a start-up company (AMKBiotek) nearby thanks to a Silab grant and to the expertise she acquired in the team.
The national visibility of the team is excellent, with 24 invitations essentially at the regional/national level. Both PIs participated in a handful of evaluations for funding agencies (Cancéropôles Gefluc, Ligue contre le cancer, the Dutch foundation FWO…) and for Hcéres. The team is well connected with clinicians and pathologists, notably at the Centre Antoine Lacassagne in Nice, and its expertise in onco-immunology is internationally recognised.
The team obtained several competitive grants, notably one ANR as coordinator (2021-2024) and two contracts from the Cancéropole Paca. The team is partner on one ANR, one INCa, one Arsep and one important European Innovative Medicine Initiative grants. Its activity was also supported by the Labex Signalife and the Idex Jedi through two PhD and one postdoctoral fellowships, respectively.

The team is very strongly involved in translational research. It contributed to clinical cohort and database establishment for patients with epidermoid cancers and it is involved in a national clinical assay on the use of Nivolumab for the treatment of Squamous Cell Carcinoma of the Head and Neck. It also developed real-time digital bio-imaging system and mass cytometry protocols to analyse human tumours. The team filed two new patents on immunotherapies against HNSCC and obtained four extensions for a former one on anti-LLT1 antibodies at the international level. It obtained two license agreements, several contracts with the industry (Galderma Nestlé, Tusk Therapeutics, Innate Pharm, BMS, Excellgene, Vaxeal) and one Cifre PhD fellowship together with PKDerm.
The PIs of the team produced some outreach videos and contributed to press articles (Inserm Mag, Nice Matin) on immunotherapy.

Weaknesses and risks linked to the context

One technician and one Inserm researcher left the team in 2016/2017. The current size of the team hinders the development of more ambitious projects.
Two PhD students left the lab with no first author publications; two out of three postdocs did not yet obtain publications as first or last authors either.
The impact of the scientific production and the international standing of the team could be improved.

RECOMMENDATIONS TO THE TEAM

- The team should pursue its efforts to maintain its outstanding level of translational research.

- The different fundamental and translational projects seem quite diverse and a more focused approach should be envisioned to fit the human resources.

- The team should seek to recruit some permanent researcher and/or technician to be able to pursue more ambitious research projects in onco-immunology.

Team 5: Molecular & cellular biology of normal & pathological cerebral aging

Name of the supervisor: Dr Frédéric Checler

THEMES OF THE TEAM

Team 5 has a long-standing interest in neurodegenerative diseases (including Alzheimer and Parkinson's disease) and extended its research to cerebral cancers (glioblastoma). It uses cellular and experimental in vivo models to study the cellular dysfunctions that take place in these pathologies and their common molecular denominators.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous committee recommended that the team increases its collaborations with IPMC teams as well as its valorisation activity and brings some of its project to the pre-clinical stage.
There was no clear improvement concerning these aspects.

It also mentioned that the future retirement of the group leader should be anticipated and this recommendation was addressed: It is proposed that two senior researchers will co-direct the team for the next contract.

Also, as recommended, the team maintained an excellent level of publications for PhD students, which allowed them to continue their career as postdocs or in the private sector.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	2
Scientist (Chargé de recherche, CR) and associate	2
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	4
Subtotal permanent personnel in active employment	**8**
Non-permanent teacher-researchers, researchers and associates	2
Non-permanent research supporting personnel (PAR)	0
Post-docs	0
PhD Students	9
Subtotal non-permanent personnel	**11**
Total	**19**

EVALUATION

Overall assessment of the team

This is a very well-established team that develops sounds and original research. Its production is excellent to outstanding both qualitatively and quantitatively. It has an outstanding international reputation and was very attractive during this contract, hosting many PhD students (17) and obtaining substantial national funding support. Its interactions with the general public and patient associations are excellent to outstanding,

Strengths and possibilities linked to the context

This is a relatively large and very well-constituted team with a long-standing interest in the aetiology of Alzheimer and Parkinson diseases and more recently in glioblastoma. Combining state-of-the-art molecular and cell biology approaches as well as in vivo preclinical models, it obtained exciting results concerning the impact a ß-secretase-derived fragment in Alzheimer disease-related syndromes, the interplay between ER-stress and mitophagy in Parkinson disease, or the role of Parkin as a tumour suppressor in glioblastoma.
Overall, its production is of very high qualitative and quantitative levels, with 35 research articles as main author and thirteen in collaborations, including several publications in the best journals of the speciality (e.g. Acta Neuropath., Autophagy, Cell Death Diff, Biol. Psy, and Mol. Psy). Among others, this has allowed to reveal a previously unrecognised mechanistic interplay between ER-stress a mitophagy, and includes the pioneering demonstration of a role of aminopeptidase A is in Aβ truncation. The team also published many reviews including a "Guidelines in Autophagy" (17). The production is well spread among the researchers of the team and the PhD students.
The team has attracted a very high number of PhD students (17) as well as three postdoctoral fellows, and it hosted two visiting foreign researchers.
The team was very well funded by national and regional institutions: it coordinated the Labex DistalALZ, one ANR and six grants from charities (France Parkinson, Fondation Alzheimer, Fondation de France) and it obtained contracts from Idex Uca Jedi and from regional authorities. It is also partner on two other ANR and one INCa grants.
The level of recognition is outstanding: the team gave more than 50 oral conferences, mostly in international settings during the period of evaluation and three PI participate in editorial committees of scientific journals (Cells, Curr. Alz. Res., Frontiers Neurosc., J. Alz. Dis., Scientific Reports). The team leader is a foreign member of the Brazilian academy of Sciences and other researchers of the team obtained the PEDR as well as one price from the Fondation Alzheimer. Moreover, several members of the team are involved in scientific committees for health foundations (Alzheimer Fondation, Fondation de France…) or in scientific boards (CoNRS 28, CSS4, ANR CS14, Hcéres SVE3, Idex Jedi, FHU OncoAge). The team has well-established international collaborations, notably with Thailand (program SIAM) and Brazil (program PHC).
The team is actively involved in interactions with the lay public, patient associations and younger pupils. It contributed to some interventions in the media (Nice Matin, FR3..) as well as to webinars and videos on social media.

Weaknesses and risks linked to the context

Despite its disease-oriented projects, the team does not seem to have very strong links with clinicians.
The team also has few interactions with industry and non-academic partners, other than a CNRS pre-maturation program for inhibitors of Aß cleavage.
Out of nine past-PhD students, one did not finish their thesis.

RECOMMENDATIONS TO THE TEAM

- This very successful team can be commended for the quality of its research. The team might strive for further funding at the international level and integrate European research consortia on Alzheimer/Parkinson diseases. The team should also try to attract more postdoctoral fellows.

- By bringing together research on AD, PD and glioblastoma, the team has developed original lines of research, but it may be difficult to maintain competitiveness in these three areas at the same time, especially with the departure of the current team leader. The future team leaders should examine the scope of their research to focus on their main strengths.

- Although this should not be done at the expense of its fundamental research projects, the team has the potential to develop stronger links with clinical research and to strengthen the economic valorisation of its discoveries.

Team 6: Lipid transport in health & diseases

Name of the supervisor: Dr Guillaume Drin

THEMES OF THE TEAM

The team aims at deciphering the molecular bases of lipid transport processes. It focuses on the elucidation of the mechanisms performed by Lipid Transfer Proteins. It intends to identify the structural elements that impart these proteins with the ability to rapidly and specifically exchange lipids between two organelles. The team has developed original methods and tools to reconstitute these systems in vitro, remaining as close as possible from the natural environment. By applying several biophysical techniques, e.g. circular dichroism, fluorescence, dynamic light scattering and microscopy, the team is able to get accurate measurements. The results are systematically confronted to cellular biology observations that are obtained thanks to the expertise present in the team.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was created in 2018. Thus, no recommendation was made in the previous evaluation since the team as it is now didn't exist.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	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)	1
Post-docs	0
PhD Students	1
Subtotal non-permanent personnel	**2**
Total	**5**

EVALUATION

Overall assessment of the team

The team has a unique expertise in the field of lipid transfer proteins and masters concepts between membrane cell biology and structural biology. Considering the small size of the team (2 FTEs), the scientific production is excellent to outstanding (15 publications in highly reputed journals, e.g., J. Cell Science, BMC Biology, Nat Commun…). Substantial national financial support was obtained. The team has an excellent international reputation, as assessed by invitations and collaborative projects. The team is also involved in very productive collaborations with other teams and has recently made a commitment in more translational/health-related/pharmacological projects.

Strengths and possibilities linked to the context

From the original discovery of sterol/PI4P exchange, the team has largely contributed to the extent of knowledge relative to the transport of lipids between organelles as well as to the plasma membrane. It develops and masters original approaches at the crossroad between cell biology and structural biology. Thanks to its original expertise, the team is involved in several collaborative ambitious projects, like the one with a group of IGBMC (Illkirch, University of Strasbourg). In this case, the team has focused on STARD3, an archetypical member of the Start family involved in breast cancer.
Considering the small size of the team (2 FTEs), the production was excellent to outstanding with fourteen publications in highly reputed journals (J. Cell Science, 2020, BMC Biology, 2021, Embo Rep, 2018, Embo J, 2020, lately JCB 2022). Importantly, the study of the yeast protein Osh6p, a representative PS/PI (4) P exchanger, has shown for the first time that a LTP can self-limit its residency time on membranes to ensure efficient lipid transfer. This study was published in Nat. Comm in 2019 and is considered as a milestone, which has led to methods and review papers (Drin, editor of 'Intracellular Lipid Transport' Methods in Molecular Biology, 2019, Front Cell Dev Biol. 2020, J Vis Exp 2021).
The reputation of the team is acknowledged by six speaker invitations in international conferences and five oral presentations in national and international meetings.
The team was successful in getting national grants as a coordinator (ANR, Exchange, 2016-2020) or collaborator (ANR Cocon, ANR MixANDMove, and Inca), for a total amount of 807 K€.
The team currently works on BAR-domain- containing proteins in *Toxoplasma gondii* in the framework of an ANR project (ANR Remind). The team is efficiently involved in training by research: one PhD student defended his thesis during the period. He contributed to six publications (three original research papers, one review paper, two methodology papers) as a first author or co-author. One PhD has started his project in 2020. Master students were also trained.
The team has started engagement in more translational/health-related/pharmacological projects with the objective to identify new anti-cancer compounds that target lipid transfer proteins or study Apicomplexan's proteins.

Weaknesses and risks linked to the context

The main weakness is the human resources of the team, which limits in particular the capacity to train PhD students (only 1 HDR). No recruitment on permanent position has happened during the period.
An identified threat is the capacity to secure proper funding resources. Consequently, the risk is to lose the unique expertise and international visibility by being more involved in collaborative projects than leading their own views. This is the risky counterpart of the opportunity.

RECOMMENDATIONS TO THE TEAM

- In terms of attractiveness, the quality of the scientific environment should make it possible to attract brilliant young researchers, doctoral students and post-doctoral students, particularly from abroad.

- A common scientific strategy linking fundamental research and translational research could make it possible to secure project financing capacities and to envisage recruitment (clinicians, engineers, etc.).

Team 7: Arf proteins, cell morphology & membrane transport

Name of the supervisor: Dr Michel Franco and Frédéric Luton

THEMES OF THE TEAM

The team investigates new biological functions regulated by members of the exchange factors for Arf6 (EFA6) family and the mechanisms associated with their activity. The work aims to characterise in-depth the intimate molecular mechanisms of action of EFA6 and Arf6 proteins to better understand their functions at the cellular, organoid or whole organism level. Different lines of research are conducted: the set-up of in vitro screens to reveal the mode of action of effectors and regulators, the extrapolation of these results into 3D epithelial cell models as well as into in vivo models. Processes involved in different biological functions are analysed: polarity, ciliogenesis, cancer, development.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous evaluation recommended a focus on a restricted number of projects, an increase of the international visibility and attractiveness of the group, a better integration of the group in IPMC and developments of the translational aspects of the research theme.

The group has recruited a permanent researcher leading a start-up project aimed to develop drugs to overcome the resistance of cancer cells to chemotherapy and is involved in the development of a clinical trial strategy. One declaration of invention concerning the use of Arf6 inhibitors for cancer treatment has been filed.

During the period, the current group members have supervised the work of five PhD students, including one in co-supervision, but no postdocs were recruited. The group still continued to work on several systems involved in different biological functions (alpha-actinin, actin, primary cilium, Numb and Wnt), but lately focused most of their efforts on two cancer projects. Its integration at the IPMC has been improved through collaboration with the team of Bernard Mari on CRISPR screening.

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	3
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	**5**
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	**6**

EVALUATION

Overall assessment of the team

The production of the group is very good to excellent with six publications where group members were leaders or co-leaders in the study. The group has an excellent national visibility and is involved in five collaborations with well-renowned groups. The team has been successful in obtaining regional or national fundings, notably lately with another ANR grant and start-up funds from Signalife Young Entrepreneur, Start-Up DeepTech, and CNRS RISE programs. The non-academic activity is excellent with a start-up project lead by a newly recruited permanent researcher.

Strengths and possibilities linked to the context

This is a relatively small team composed of five permanent members, one assistant-engineer and three PhD students (including one in co-supervision). The team has an extensive expertise in the biological functions regulated by Exchange Factors EF 6A and their substrates Arf6. During the period, they show that EFA6 proteins regulate lumen formation through a-actinin 1, that EFA6A regulates early steps in ciliogenesis, that the C-terminal domain of EFA6A interacts directly with F-actin and assembles F-actin bundles, that the C-terminal domain Arf6 is necessary for the senseless expression in response to wingless signalling during Drosophila wing development. Concerning the projects related to cancer, they showed that Chlortetracycline is an Arf inhibitor that decreases the Arf6-dependent invasive properties of breast cancer cells and reveal an EFA6B-regulated molecular mechanism that controls the invasive potential of mammary cells.

The scientific production is very good to excellent with nine original articles published since 2017, six as corresponding authors, in journals including one in Nature Communications (2021), two in Journal of Cell Science (2018, 2021), one in Biology Open (2021) one in Scientific Reports (2019) and one in Molecules (2021).

The team has established several collaborations at the national level with groups that have expertise in biological systems associated to various EF6A protein (CRCM-Marseille, I2BC-Gif/sur/Yvette, Imagine institute-Paris, - Nice).

The team has obtained national (ANR and ARC in 2016) and regional (2021) fundings. Another ANR grant and substantial funding for a start-up company project (Signalife Young Entrepreneur, Start-Up DeepTech, and CNRS RISE programs) have been obtained lately.

The group has recruited a permanent researcher to set up a start-up and develop translational aspects of the research theme, by developing inhibitors of the patched receptor (working as efflux transporter limiting the effect of chemotherapies against cancers of different origins). This excellent recruitment is expected to catalyse the efforts of the group towards translating their findings into the clinical setting.

During the period, current group members supervised five PhD students, including a co-supervised one. Each student published as first or co-first author and as co-author of other publications.

Weaknesses and risks linked to the context

The visibility of the team is modest at the international level as there was no invitation to international meetings (two invited seminars in the same university in Japan).

RECOMMENDATIONS TO THE TEAM

The team should capitalise on its positive dynamics by leveraging the full potential of synergizing projects related to EFA6/Arf6, Patched, and the process of tumour dissemination, by further intensifying the obtention of national and if possible international fundings, by continued training of M2 internships and PhD students, and by attracting postdocs.

Team 8: Immune system, brain and peripheral nerves

Name of the supervisor: Pr Nicolas Glaichenhaus

THEMES OF THE TEAM

The team has two clearly defined objectives. Firstly, to elucidate the link between the autonomous immune system, and more specifically the splenic and pancreatic nerves, and the autoimmune response and secondly, to decipher the gut-brain-immune axis, and more specifically to understand how microbial metabolites and cytokines impact behaviour. The team has also contributed to find new immune biomarkers for selective diagnosis of psychiatric disorders. The two research lines, which were led by two distinct groups in the team, have progressed independently during the period.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

·*Document newly obtained expertise by publication*
The team has achieved the goal of the successful establishment of new expertises in neuroimmunology and the gut-brain axis documented by publication of major discoveries, with members of the team as first and last authors,

·*The team might profit from inclusion of foreign scientists.*
Two PhD students and one postdoc were on international mobility.

·Involve team in science policy and local activities to disseminate science.
The situation seems unchanged with no record of scientific expertise provided to the community. Several team members are nevertheless involved in teaching duties and associated scientific management activities. Outreach activities were excellent.

·*Consider new scientific focus for future recruitments.*
One neurobiologist and one developmental biologist specialised in brain development are already part of the team, in line with its scientific strategy.

·*Take care of development of younger team members to independency.*
Two research lines organised as two groups are led by senior team members that publish their work as main authors and that have proven their capacities to develop their own projects. Funding however still heavily relies on the current team leader and only one tenured scientist has records of invitations to international conferences.

·*Improve integration into IPMC structure*.
The team is now well included in the transversal axis 2 coordinated by a team member.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	2
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	3
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	0
Subtotal permanent personnel in active employment	**6**
Non-permanent teacher-researchers, researchers and associates	3
Non-permanent research supporting personnel (PAR)	4
Post-docs	0
PhD Students	3
Subtotal non-permanent personnel	**10**
Total	**16**

EVALUATION

Overall assessment of the team

New research lines started in the last period are now well established and ensure the inclusion of the team in the unit's scientific strategy. The team has an outstanding scientific production with major discoveries published in high visibility journals (Nature Biotech, Microbiome…). The team had outstanding translational activities with 4 patents for biomedical treatments or diagnosis and a successful collaborative project with a company (Galvany, a spin-off of GSK). Team members had an excellent supervising activity (7 PhD students and 4 Post-doc). Given their research interests, the team members are well positioned to be even more involved in interactions with the larger public.

Strengths and possibilities linked to the context

The team has successfully shifted its focus during the last period from mucosal immunity to a nerve-brain and gut-brain versus immunity axis with high impact in the biomedical field. Team members develop a multidisciplinary approach covering immunity, neurobiology, epidemiology and applied mathematics with high impact for both treatment or diagnostic/prognosis for several pathologies, including psychiatric disorders. The team members have produced 58 publications including 29 as first/last authors in very well-regarded journals (Brain Behav Immun, BBI Health, Mol. Metab., eBioMedicine, Stem Cell, translational psychiatry). Major discoveries from the team's own projects have been published in high-profile journals. The demonstration that the electrical stimulation of the pancreatic nerve can inhibit type I diabetes was published in Nature Biotechnology in 2019 and the use of cytokines in the cord serum at birth for the prognosis of anxiety/depression in young children, in Biological Psychiatry, 2019. Finally, the team showed in an original study that the microbial metabolite p-Cresol induces autistic-like behaviors in whole organism model by remodelling the gut microbiota (Microbiome, 2021).
Team members have obtained funding at the European level with a very competitive ERA-NET grant and an MSCA individual fellowship for postdoctoral in-coming mobility. At the national level, the team participated to three ANR, including one as coordinator. Part of the team funding has been obtained by medical foundations and local institutions: Uca, Paca. Funding was also received from the SATT Sud-Est. Principal investigators have

contributed to the project visibility by presenting their research at several national and international congresses. The group leader has received the 'Marcel Dassault price'.
Team members have supervised seven PhD students during the period: four have obtained their PhDs, two are ongoing and one did not finish. The four graduated students are now postdoc fellows abroad. Two of the students were co-supervised with the 'laboratoire d'informatique, signaux et systèmes I3S' to develop applied mathematical approaches. Four postdoctoral fellows have joined the team during the period. Two of the PhD students and one postdoc were on international mobility. All the early stage researchers are co-authors of the team publications. Team members are involved in clinical studies including one coordinated by the team leader.
The team has a close collaboration with a company (Galvany, a spin-off of GSK) resulting in consequent funding, three co-authored publications, two patents and ongoing clinical trials. The team has filed five patents during the period, notably two of them are licensed, showing the high relevance of their research in the medical field. Team members disseminated their research to the general public by press-articles, one web-TV show and by participation to two conferences organised by patient associations.

Weaknesses and risks linked to the context

The international visibility of the team could be even better given the outstanding quality, originality and biomedical impact of their research.

RECOMMENDATIONS TO THE TEAM

- Increase participation of the team members to conferences would be positive to further improve visibility of the research projects.

- Attention should be paid to funding because this was still mainly supported by the team leader in the last period who will retired for the next contract.

- Increased involvement with the public and patient associations, if time permits, because it seems of obvious interest given the closeness of the team to the medical field, particularly concerning mental health.

Team 9: Metabolism and functions of membrane lipids

Name of the supervisor: Dr Takeshi Harayama

THEMES OF THE TEAM

The team focuses its research on lipids and more precisely on the metabolic regulation of membrane lipid composition and the biological functions of the hydrophobic acyl-chains of lipids.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

This point does not apply since it is an emerging ATIP-Avenir team that just started during the pandemic crisis.

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

EVALUATION

Overall assessment of the team

By focusing on the acyl-chains of lipids, this ATIP-Avenir team addresses its research topic on lipids with a quite original approach, for which it develops, with its former collaborators, innovative tools (CRISPR-Cas9 and chemical biology of lipids). Although it is too early to assess the scientific impact of this team, the committee was impressed by the quality of the discussion with this new young PI and the research developed in his team looks very promising.

Strengths and possibilities linked to the context

The team addresses the biological function of lipids through the study of acyl-chains, in contrast to many labs that focus on lipid head groups, and has therefore a very original approach in this field of research.

The PI has an excellent track record of publications in the lipid field. In particular he contributed to the functional analyses of lysophospholipid acyltransferases (Faseb J. 2017; Faseb J. 2021), and engineered lipids that can be chemically modified to be targeted to specific organelles upon light illumination (eLife 2018). He has co-authored a review with its former supervisor (Harayama and Riezman, Nat Rev Mol Cell Biol, 2018) that has been highly cited (788 times).

The toolkit developed by the PI with his collaborators (a combination of chemical biology and genetics) is quite innovative and should put this new team at the forefront of the research in lipid metabolism, leading to the discovery of unknown roles of lipid acyl-chains.

Currently, this new team is not involved in partnership contracts with industry, but the PI has previously collaborated with a company to develop pulmonary surfactant-based drugs (Harayama et al, J Lipid Res 2015).

Likewise, the team has not been engaged in citizen participatory science activities so far, but it is noteworthy that the PI formerly participated to the 'Ecole Japonaise Complémentaire de Genève' to educate the general public to the work of scientists.

Weaknesses and risks linked to the context

This is an emerging ATIP-Avenir team and the young PI just got a position at the CNRS as a CRCN. So he is the only permanent member in this team.

RECOMMENDATIONS TO THE TEAM

The team will now need to recruit additional staff, hopefully on permanent positions. Some help from the unit would certainly be welcome in this matter, either by re-allocating an engineer already present in the unit to work in this team or by hiring an engineer on a non-permanent contract. Given the whole budget of the unit, this appears within reasonable reach.

The committee wishes a lot of scientific success to this highly promising new team.

Team 10: Neuropeptides, brain diseases and therapeutics

Name of the supervisor: Dr Catherine Heurteaux and Jean Mazella

THEMES OF THE TEAM

The team is focusing on the relationships between stroke & post-stroke, environment and diabetes and their consequences on major depression induction. The ultimate purpose is to develop pharmacological treatments (via spadin, a peptide identified as an antidepressant, and spadin-derivatives) and the diagnosis of depression and post-stroke depression. In addition, the team explores spadin derivatives as new tools against diabetes.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS *REPORT*

The main recommendation of the previous committee for this team (resulting from the fusion of 2 teams of the unit) was to increase the quality of the journals in which the team publishes.
The quality of the journals has remained relatively similar but the number of articles and journals has remained stable which is quite remarkable for a team with three retiring members (in 2023). As detailed below, the citation rate over the last period is excellent, largely compensating the quality of the journals, which can also be viewed as a publication strategy by itself.

Two other minor recommendations were the recruitment of postdocs from abroad and the absence of ERC. These two points have remained unchanged although Team 10 has recruited three postdocs over the last period.

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	3
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	**6**
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	1
Post-docs	0
PhD Students	2
Subtotal non-permanent personnel	**3**
Total	**9**

EVALUATION

Overall assessment of the team

The team focuses on the application of spadin for the treatment of stroke/post-stroke depression, a major health burden. The teams's international impact on this topic is documented by very good to excellent publications. The team has an excellent valorisation activity, deeply involved in translational research with several patents, and is associated a biotech creation (3P3D). The team has a pivotal position in the IPMC with tight collaborations (and related publications) with four other teams. Team members have an excellent academic supervising activity since all PhDs and postdocs got first-author publications.

Strengths and possibilities linked to the context

The team is very well established in the institute with more than fifteen years of experience, and tight interactions with other teams of the IPMC (see below). The research lines are of a crucial importance since the team aims to identify therapeutic molecules (mostly spadin and spadin derivatives, e.g. mini-spadin) for treatments for post-stroke depression, which is a major societal burden. During the 2016-2021 time period, the team members were invited to give talks (x13) at a significant number in international workshops, meetings and institutes (in EU, Japan, China and USA). This illustrates the excellent position of the team research on the international scene of their domain. Members of the team participated to expertise (x14 during the period 2016-2021) for national and international organisations and for public administrations.

The high number of publications (35) reflects a very good to excellent activity and should be acknowledged; 25 out of the 35 original papers have a member of the team as first, last and/or corresponding author. These publications, although not in notoriety journals, are highly impactful with 525 citations. It should also be noted that eleven of the published papers have been achieved in collaboration with four other teams of IPMC, highlighting an excellent integration and pivotal position in the institute. Furthermore, the number of reviews (14) is quite impressive knowing that six originate directly form the team. This effort is notable and obviously precious for the international visibility of the team. The ratio of publications per postdoc (x2 with 8 articles) and PhDs (x4 with also 8 articles) reflects the great care of the team senior researchers to provide an efficient and rigorous mentorship and follow-up.

The team has an excellent (and successful) involvement in valorisation of their research lines and in particular developing therapeutic applications of spadin (or spadin derivatives) via collaboration with non-academic societies such as Cerb (France) and Moleac (Singapore). These two collaborations were successful since they were funded with an ANR grant which allowed establishing a license of their patents and the creation of a biotech (Public Private Partnerships for Drug Discovery and Development, 3P3D) devoted to the development of the spadin/mini-spadin for clinical trials; and also the development of new formulations of active molecules (MLC601 and MLC901) derived from traditional Chinese medicine for treatments for stroke and traumatic brain injury. The team follows an active policy to protect intellectual property via patent filings, mainly with Cerb and CNRS. In translational interactions, the team established numerous medical collaborations (CHU Marseille, Lille, Nice, Psychiatric Hospital in Breccia, Italy), including for pre-clinical trials.

Weaknesses and risks linked to the context

The targeted journals for publication could have higher international visibility. A possible strategy would be to assemble several papers for more complete packages. This may help to achieve even better visibility, knowing that the key factor should not be the impact factor but the number of citations (i.e. 525) which is very good and highly satisfactorily for papers recently published. Nevertheless, more visible papers and increased participation in meeting and invited talks should help gaining international visibility.

RECOMMENDATIONS TO THE TEAM

The team should greatly benefit of more visible publications, possibly by building full package papers instead of slicing projects into several publications. Also, the team 10 should hire more PhDs students especially with their excellent positioning with non-academic partners.

Team 11: Molecular and Integrative Mechanobiology

Name of the supervisor: Dr Eric Honoré

THEMES OF THE TEAM

The team is investigating the molecular and cellular mechanisms underlying mechanotransduction with a special emphasis on the contribution of mechanosensitive K2P and piezo channels to pathological conditions such as malaria, obesity, hypertension and acute kidney injury.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The desire to keep a relatively small team can interfere with the capacity to follow all the scientific questions raised by the new findings.
The team has maintained excellent scientific production on various aspects of mechanotransduction thanks to contribution of all team members. Studies on piezo channels and their potential anti-malarial role have been a main focus involving collaborations with internationally recognised scientists including a recently awarded Nobel Prize in Medicine (A. Patapoutian).

The team moves towards translational work (e.g. with obesity or malaria) identifying links with potential private companies would be helpful.
The search for novel Piezo1 activators with antimalarial properties received financial support via the CNRS prematuration program and one member of the team is a member of the ChemBioFrance executive committee. No current partnerships with private companies are mentioned.

Despite the recommendation of the previous evaluation committee, the contribution of the team to PhD supervision and postdoctoral researcher training remains limited as the team (3 tenure scientists) only hosted two PhD students and two postdoctoral fellows during the 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	2
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	**4**
Non-permanent teacher-researchers, researchers and associates	1
Non-permanent research supporting personnel (PAR)	0
Post-docs	0
PhD Students	2
Subtotal non-permanent personnel	**3**
Total	**7**

EVALUATION

Overall assessment of the team

The originality and quality of the research is acknowledged by the team's excellent publication record and excellent capacity to secure financial support. The team has gained outstanding recognition for its research activity on the mechanisms underlying the activity of mechanosensitive ion channels as indicated by an established network of international collaborations with world leading scientists and review articles in very high-profile journals. The implication of the team in training actions and interactions with the socio-economic environment may need to be further developed.

Strengths and possibilities linked to the context

During the period, the team further exploited the discovery of the mechanosensitive properties of ion channels. The team has established a strong collaborative network locally with several other teams at IPMC, nationally (Infectiopole Sud, Montpellier) and internationally with renowned scientists (Germany, Hong Kong) including a recently awarded Nobel Prize in medicine. The international recognition of the team is also acknowledged by three reviews in excellent journals (Trends in Pharmacological Sciences, Cell, Nature Reviews Nephrology) and several invited seminars. The team has been very successful in securing international (Human Frontier Science Program) and national funding (4 ANR among which 2 as coordinator, Team FRM, Institut de France, Mediterranee Infection, Labex, Idex) and has also been the recipient of a prematuration contract to evaluate piezo1 as a drug target in malaria. A partnership has been established with the University of Hong Kong and, more recently, the University of Singapore, which should offer access to more training opportunities. During the period, the team also developed computational methods (SENSAAS Software) and generated databases (E-DRUG3D) for virtual screening and de novo molecular design, drug re-purposing and knowledge-based design of drug-like compounds. In addition, one team member is part of the executive committee of ChemBioFrance and the director of the GDR Big Data.

The team has an excellent publication record with eighteen original articles published in very high-profile journals (Cell, Nature communications, Cell Reports) or journals of reference (e.g. Journal of Biological Chemistry, Neuropharmacology, Pflugers Archives). Of note, about two third of the articles are signed as first, last or corresponding author by the team members.

Weaknesses and risks linked to the context

Training actions and links to the socio-economic world are lacking which might hinder the capacity of the team to fully exploit its outstanding scientific discoveries. Moreover, limited interactions with clinicians and private companies could hamper the development of translational perspectives. One might also note the absence of involvement in events towards the general public.

RECOMMENDATIONS TO THE TEAM

As already mentioned in the previous evaluation, the team should aim at increasing its implication in the training of young researchers (PhD students and postdoctoral fellows) and should further develop its capacity at securing funding for the translational aspects.

The team should also keep on strengthening the integration of the in silico expertise within a multidisciplinary approach to decipher the implication of mechanotransduction in physiopathological conditions.

Team 12: Mechanisms of gene regulation in physiopathology

Name of the supervisor: Dr Enzo Lalli

THEMES OF THE TEAM

The team studies the development, the function and the pathology of the adrenal gland by using integrated approaches from basic sciences to medical applications. The team has expertise in molecular and cell biology methods, develops genomic tools and models to initiate pharmacological and clinical studies.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team should deepen and develop more ambitious work and aim to publish in high impact journals. Thoughts and self-evaluation should take place to point out weaknesses and plan for potential improvements.
This recommendation has not been addressed.

To keep their reputation and reach a European recognition (including getting funded) efforts and active actions should be considered and taken. Efforts to attract PhD students and postdocs, as well as participation in European projects should be considered.
This recommendation has been addressed as the team belongs to an European Laboratoire d'Excellence and secured European FP7 funding.

Better management of the team and efforts to attract PhD and post-doc should be considered.
Not clearly considered yet in terms of management (one PhD student) and with no HDR from other permanent members 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	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	0
PhD Students	1
Subtotal non-permanent personnel	**2**
Total	**6**

EVALUATION

Overall assessment of the team

During the period, the team had a very good to excellent scientific production with 36 papers including 10 research papers authored as first or last/colast (Science Signaling 2017; Clinical and Translational Medicine 2021). The team has an excellent visibility (PI invited over 10 meetings including European Society of Endocrinology) and has been labelled European Centre of Excellence for research in adrenal tumours. Their recognition is excellent with high fund-raising (~1800 kE, 4 ANR, 1 ARC, 1 Cancéropôle, 1 Labex, 1 FP7). The non-academic activities remain good and may need to be developed.

Strengths and possibilities linked to the context

During the period, the team had a very good to excellent scientific production with 36 papers (18 research, 18 reviews cited 393 times) including ten research papers authored as first or last/colast (Science Signaling 2017; Oncotarget 2017; Clinical and Translational Medicine 2021), among journals specialised in endocrinology mainly.

The team has an excellent visibility in the field shown by frequent invitations to present at international meetings in the domain of adrenal physiopathology (PI invited over 10 meetings including Adrenal Cortex Meeting, ACC Meeting, ENS@T Annual Meeting, Meeting of the Endocrine Society, European Society of Endocrinology Meeting). They also are members of journal Editorial Boards (such as Journal of the Endocrine Society; American Journal of Cancer Research; Frontiers in Molecular and Structural Endocrinology). The team has been labelled European Centre of Excellence for research in the field of adrenal tumours and they have several international collaborations (CNRS co-joint project with Pequeno Principe Research Institute and St. Jude Children's Research Hospital). Their recognition is also demonstrated by excellent fund-raising (around 1800 k€ over the period) with 10 contracts as coordinator (4 ANR, 1 ARC, 1 Cancéropôle, 1 Labex, 1 FP7) and three are currently running.

The non-academic activities of the team seem to be very good but no details have been provided on this matter and may need to be further developed.

Weaknesses and risks linked to the context

The team published a high number of publications but with a moderate visibility. The risk is a decrease in visibility and funding at midterm. In addition, no tech transfer has been performed during the period that might also limit the funding opportunities and attractiveness of the team.

RECOMMENDATIONS TO THE TEAM

The committee recommends to target publications in more generalist journals to broaden the visibility of the excellent science performed in the team.

Also, the non-academic aspects need to be clearly developed in the near future.

Team 13: Molecular physiopathology of phospholipases A2 & their mediators

Name of the supervisor: Dr Gérard Lambeau

THEMES OF THE TEAM

The team studies the functions of secreted phopholipases A2 (sPLA2s) and the phospholipase A2 receptor PLA2R1 in different physiological and pathological contexts. In particular, the team aims to determine the role of PLA2s in inflammation and the many associated pathologies such as host defence against pathogens, reproduction, cell proliferation and cancer. The team also aims to understand the role of PLA2R1 in membranous nephropathy (MN), which is a rare autoimmune kidney disease.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

1 - Consider focussing on independent projects and taking a leadership role in collaborative ventures.
Although the scientific output of this team remains high, it is still dominated by numerous collaborations in which the senior author(s) are not part of the team. The research themes are still rather dispersed due to its multiple collaborations.

2 - Recruit more international postdoctoral staff.
The team recruited two postdocs during the evaluation period, including one international researcher.

3 - Further industrial sponsorship could support staff positions and enhance the research output of the team.
This recommendation has been fully followed. Three patents were filed or extended, one is pending licensing, older patents have been licensed leading to the marketing of products sold worldwide. The team had patents, licensing and marketing of diagnosis kits with Aterovax. Collaboration with Diaccurate has provided funding for post-docs, engineers and reagents over 8 years, with co-publications in JCI.

4 - Sufficient number of skilled technical staff.
Still only one staff technician but one postdoc in the lab was hired by CNRS as Research engineer and works in the team since then. Others were employed on non-permanent contracts.

5 - Little evidence of PhD student achievement in the form of publications.
This point has been satisfactorily addressed as four Master students, four PhD students and two postdocs have contributed to publications. These categories of researchers are first or co-first authors of 30 publications.

6 - Funding appears to be patchy.
Excellent level of funding: ANR PRC as coordinator, FRM label, AFM Telethon, Fondation Maladies Rares, in addition to contracts with industry.

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	3
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	**7**
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	3
Post-docs	0
PhD Students	0
Subtotal non-permanent personnel	**3**
Total	**10**

EVALUATION

Overall assessment of the team

The scientific production is very good to excellent, considering very good articles whose first/last authors are from the team, and some excellent articles published with collaborators, and three patent filings. The attractiveness is excellent to outstanding when considering the PhD student supervision, the contracts and prizes that were obtained. The technology transfer activities of the team are rightfully outstanding, and its participation to outreach activities is excellent.

Strengths and possibilities linked to the context

The team focused on the molecular mechanisms by which PLA2R1 influences PLA2R1-associated membranous nephropathy (MN). The team is also studying the role of PLA2s and associated signalling pathways in brain function and the impact in depression, psychosis and autism.

The scientific production is very good for six permanent researchers with articles for which team members are first and/or last author. These articles are published in recognised journals in their field such as Clin J Am Soc Nephrol, Kidney Int, J Am Soc Nephrol, Metabolism. The scientific activity of the team is marked by a large number of excellent publications where the team has provided technical expertise to collaborators. Some of these articles are published in more generalist journals, such as J Clin Invest (2), Nat Chem Biol and Nat Comm. In addition to these publications, the team has filed three patents.

The team has been successful in several competitive national calls for projects (ANR PRC as a coordinator, FRM labelling, AFM Telethon, Fondation Maladies Rares, PHRC National 'PMMN', Personalised medicine for the treatment of extramembranous glomerulonephritis…), as well as contracts with industry. The team thereby is well funded.

During the reporting period, the team welcomed four PhD students, whose supervision involved three researchers of the team. All four students have defended their PhD thesis. There have been no PhD students

recruited since the last defense in 2019. All the PhD students were funded by doctoral contracts, indicating an excellent level of success in these competitions. The training activity is very intense, judging by the large number of trainees. The team has also attracted two postdocs during the period.

The team members have an excellent to outstanding visibility as evidenced by their invitation to national (1 CSS4 member and 1 S25 member over the period) and international (2 SAB in Brazil and UK for the team leader) expert committees. Furthermore, team members participated in 52 scientific events, with more than 20 on invitation. The group leader also organised one international meeting. Of note, the group leader was awarded the Senior Prize of the French Kidney Foundation (2019) and the Prize of the Jean Valade Foundation, Fondation de France (2020).

The team outstandingly contributes to the society. The team has filed three patents, one of which to be licensed very soon by the company Euroimmun to market a detection kit for the diagnosis and prognosis of membranous nephropathy. The team also cooperated with the company Aterovax and patented antibodies to develop detection assays for sPLA2-IIA in patient sera. These assays have been sublicensed to companies in Germany (Concile GmbH), UK (Randox) and the US (Zeus Scientific).

Several members of the team contribute to scientific outreach activities in podcasts or by participating in events such as the 'semaine du cerveau', 'fête de la science', and the 'cordées de la réussite'.

Weaknesses and risks linked to the context

The absence of PhD students since 2019 could affect the dynamics of the team. However, one student has been hired as a PhD student since June 2022.
Although the group leader has undeniable recognition in his field, he rarely occupies senior author positions that would better demonstrate his leadership on projects.

RECOMMENDATIONS TO THE TEAM

The team's scientific production would benefit from more publications in high visibility generalist journals on a few emblematic studies of the team, even if it means putting a little less effort into the collaborations, of which there is a very high number.

The team should welcome more PhD students.

The committee welcomes and encourages the team to maintain its transfer activity at an exceptional level by filing patents and obtaining contracts with industry.

Team 14: Molecular physiology and pathophysiology of ion channels

Name of the supervisor: Dr Florian Lesage

THEMES OF THE TEAM

Since the discovery by the team of the two-pore-domain potassium channels (K2Ps), this team has been involved in in-depth characterisation of these membrane proteins to understand their electrophysiological and pharmacological properties, and also their subcellular localisation. The team notably studies their capacity to form heterodimers and their functional consequences.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The relatively high ratio of permanent staff to PhD students and postdocs means that permanent staff may not have opportunities to supervise PhD students.
A new HDR has been obtained in the team so it should broaden the opportunities among different team members to supervise PhD students.

The effort should be made to seek a continuation to the ICST network after the end of Labex in 2019.
The ICST network Labex has been extended until 2024.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	3
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	**5**
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	1
Post-docs	0
PhD Students	1
Subtotal non-permanent personnel	**2**
Total	**7**

EVALUATION

Overall assessment of the team

This team has a very strong expertise on channel electrophysiology with publications in excellent to outstanding journals, and an outstanding visibility in its field of research. They have a collaboration with a Japanese company and with the Taiwan mouse clinic to exploit the models developed in the lab so their interaction with the socio-economic world is equally outstanding.

Strengths and possibilities linked to the context

The team possesses an outstanding expertise on the function of K2Ps channels. They produced in vivo models to better understand their physiological role and their possible implication in pathology (e.g. human migraine). They have thus shown that heterodimer channels have unique regulatory properties as compared to homodimers and their specific pharmacological properties might be exploited for the search of new medicines. Hence, TREK1 or TREK2 interact with Tresk to form heteromeric channels involved in human migraine, while the activation of TREK1 may represent an alternative analgesic strategy to the use of opioids with potentially less side effects. Importantly, some of these channels have a specific intracellular localisation, e.g. TWIK2 to lysosomes to impact morphology and autophagy. TWIK1 shows the uncommon property of dynamic ionic selectivity.

The production of the team is excellent to outstanding as its members published eighteen articles (plus one in BioRxiv) during the period under evaluation, with seven where the principal author is a member of the team *(Nature Comm., PNAS, J.Med Chem., Front. Mol. Neurosci. , J Mol Cell Cardiol; Front. Pharmacol) plus eleven publications in collaboration (including Neuron, Nat Comm, Cell Rep, PNAS…).*

The visibility of the team is outstanding: invitations to give seminars at national and international meetings (e.g. International symposium on recent advances in biochemical sciences, Taiwan; 6th International Ion Channel Conference, Qingdao, China…), and several national or international collaborations with leading scientists (e.g. Stephen Tucker, Oxford University; Jamie Vandenberg, Sydney University; Soren Olesen, Copenhagen University; Ulrich Zechner, Mainz University…). The PI is the scientific head of the Labex ICST and has/had several duties in managing the research at the national level (CoCNRS section 28, president of the CoCNRS CID 54, 'Chargé de mission'…). The team is very well financed with grants from LabEX ICST, ONO pharmaceutical, FRM 'team labelisé', two ANR and one FFC.

Regarding the interaction with the socio-economic world, they have deposited two patents on TREK openers with analgesic properties and on modulating agents with anti-migraine properties. In addition, they have a tripartite collaboration with a company in Japan (ONO Pharma) to develop new KO and KI models, and characterise them with the Taiwan Mouse Clinic to identify new drugs and new therapeutic targets.

The team has been outstandingly involved in public dissemination of scientific knowledge with various participations: 'la Semaine du Cerveau', science festival, public lecture on ion channels (Science pour Tous), visiting high schools each year to present the profession of scientist and to explain why science is important for the future of our society. PhD students of the team also provide guidance to high school students in Vallauris or Sophia-Antipolis as part of the 'coordées de la réussite'.

Weaknesses and risks linked to the context

As mentioned in the report, the downside of the collaboration with industry is that it can hamper the publication of the results.

RECOMMENDATIONS TO THE TEAM

This team should continue on the same track of scientific excellence.

Team 15: Ion channels and pain

Name of the supervisor: Dr Eric Lingueglia & Emmanuel Deval

THEMES OF THE TEAM

The team studies acid-sensitive ion channels (Asics), which are excitatory cation channels activated by extracellular protons, and two-pore domain K+ channels (K2Ps), which are inhibitory potassium channels, both of which are targets for new drugs against chronic pain. The first line of research aims to understand the properties and regulation of Asic channels and their implications in pain. The second line of research consists of developing pharmacological tools for Asic channels based on structure/function studies.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

1 - The team should consider collaboration with foreign teams for translation of their compounds to clinic.
The team has set up an international consortium with physicians in France and Sweden (Jurczak et al., Pain 2021; Jacquot et al., Pain in 2022).

2 - Membership in collaborative research programs, international visibility.
International consortium with physicians, France-Taiwan international research.
3 - Interaction with the cultural environment.
Strong interactions with the general public: brain awareness week on the Côte d'Azur, course at the Muséum National d'Histoire Naturelle, directs 'cordées de la réussite' since 2012.

4 - Increase the number of post-doctoral researchers.
The team employed two postdocs during the evaluation period.

5 - Continue to ensure that training.
4 members of the team have supervised PhD students during the reference period.

6 - Close links with groups experienced with clinical translation of small molecules.
Based on a patent WO/2012/022894, and within the framework of the ANR-17-CE18-0019 'Development of a natural peptide as a new non-opioid analgesic' (2018-2022), the team collaborated with the CEA-Paris Saclay in order to further characterise mambalgin-1 with the short-term objective of filing an 'improvement patent'.

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	1
Non-permanent research supporting personnel (PAR)	0
Post-docs	0
PhD Students	2
Subtotal non-permanent personnel	**3**
Total	**10**

EVALUATION

Overall assessment of the team

The scientific output is excellent with articles published as first or last author in Embo J, J Neurosci, Pain, for example. The attractiveness is excellent to outstanding when considering the PhD student supervision and the contracts obtained. The participation of the team to technology transfer and outreach activities is excellent.

Strengths and possibilities linked to the context

The team remains a strong player in its main area of research on the function, regulation, pharmacology, and pathophysiological roles of Asic channels in pain. To develop its research, the team combines molecular and cellular approaches, behavioural experiments and electrophysiology.

The team collaborates with mathematicians on in vivo recordings of spinal cord activity. The team also collaborates with clinicians on the pathophysiological roles of Asic channels, which has led to concepts on the regulation of these channels by LPCs. The establishment of an international consortium with clinicians in France and Sweden has also enabled the team to show the involvement of Asics and LPCs in chronic pain associated with rheumatic diseases.

The team's pharmacological activity consists of exploiting the properties of natural snake venom toxins to develop pain-inhibiting drugs. The team continues to work on mambalagin-1, which they discovered in 2012.

The scientific production is excellent for a team comprising five permanent researchers and one professor. The team published 20 original articles during the period of reference. Articles with first, last or corresponding author from the team were published in highly visible generalist journals (Embo J, 2016), and regularly in recognised journals in the team's field of expertise: pharmacology (Br J Pharmacol, 2018; Neuropharmacology, 2017), neurosciences (J Neurosci, 2016 and 2021; Neuroscientist, 2021) and pain (Pain, 2016 and 2022).

The team's level of funding is excellent with four ANR contracts recorded over the reference period. We should also add two France-Japan international research contracts funded by the Hubert Curien/IRN CNRS programs. The team has also obtained funding from local programs such as Idex and Labex. Most of the permanent members contribute to the funding of the team.

During the reporting period, the team welcomed seven PhD students, whose supervision involved four researchers of the team. five of the seven theses have already been defended. The majority of PhD students are funded by doctoral contracts, indicating an excellent level of success in these competitions. The training activity is very intense, judging by the very large number of trainees. The team has also attracted two postdocs during the period.

Team members participated in 42 scientific events, thirteen of which were by invitation. They also organised around ten international meetings.

The team is very active in communicating its research to the general public and schools. We can mention the organisation of popular events such as 'Brain Week on the French Riviera', 'Researchers welcome patients', the organisation of a conference-concert 'How does our brain perceive works of art? ', 'venomous and poisonous animals' which is a training at the Muséum National d'Histoire Naturelle in Paris, and the Ministry of Education's program 'Towards successful scientific studies'.

Weaknesses and risks linked to the context

The translational research activity could certainly be further developed to exploit in particular the economic potential of mambaligin-1.

RECOMMENDATIONS TO THE TEAM

To maintain its international visibility, the team should publish a little more regularly in generalist journals and not only in journals which, although recognised, are intended for specialist communities. The committee encourages the team to continue its efforts to exploit the medical and economic potential of mambaligin-1.

Team 16: Pathophysiology of voltage-gated Na+ channels and neuronal excitability

Name of the supervisor: Dr Massimo Mantegazza

THEMES OF THE TEAM

The main research axis of the team focuses on the pathophysiological role of voltage gated Na+ channels using a multiscale approach at molecular, cellular, system and behavioural levels that also includes complementary in silico modelling. The team is also interested in better understanding how maladaptive changes in the Gabaergic network activity contributes to the pathological state.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous evaluation recommended to strengthen the opportunity of career development for all permanent team members. Accordingly, the publication strategy better included other team members in senior authorship position, and several team members participated to network meetings.

A technician has been recruited in 2019 for the management of the colonies and genotyping, as recommended during the previous evaluation

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	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	**5**
Non-permanent teacher-researchers, researchers and associates	3
Non-permanent research supporting personnel (PAR)	0
Post-docs	1
PhD Students	2
Subtotal non-permanent personnel	**2**
Total	**7**

EVALUATION

Overall assessment of the team

During the period, the team has pursued its excellent work to better decipher the physiopathological roles of ion channels and excitability of neuronal networks. The originality and quality of the research team is acknowledged by the excellent publication record, excellent support from national funding, strong collaborative network, participation to European programs and international recognition of the team leader. The team also actively participates to actions towards the society through strong connections with associations of patients and activities towards scholars.

Strengths and possibilities linked to the context

The team pursued its work to better decipher the physiopathological roles of ion channels, mainly Na+ voltage gated channels, and excitability of neuronal networks, mainly Gabaergic, together with their contribution to several human disorders including Dravet syndrome, migraine and ASD. The team members have complementary expertise and develop an original state-of-the-art approach that encompasses in silico and multiscale analysis with the ultimate aim of identifying therapeutic strategies. A strong point of the team's research is the use of in vivo preclinical models, neuronal cultures and patient-derived iPSCS to optimally address the molecular mechanisms underlying the development of the pathological state. This has been partly made possible through the development of excellent local, national and international collaborations, which has also led to enlarge the initial scope of the research interests to genetic rare diseases such as Rubinstein-Taybi syndrome, the ataxia telangiectasia, or X-linked intellectual disability.

The team leader has excellent national and international recognition (several invitations to workshops, conferences and schools, e.g. Am. Epilepsy Soc., Congress of the Eur. Dravet Syndrome association, Workshop on Epileptic Encephalopathies, Intern. Symp. on Ion channels and Channelopathies) and by his editorial activity as associate editor for Frontiers in Molecular Sciences and review editor for three Frontiers journals. The team members are also actively participating to local and national scientific networking and the team leader organised two workshops. The team benefits from excellent public funding at international (participation to three European contracts, three contracts as leader), national (2 ANRs, 5 contracts with associations) and local (2 Labex, 3 Idex) levels, however, almost exclusively through the team leader. The team also secured a two-year contract with the pharmaceutical company Lundbeck. Two team members participated in ethic committees (Ciepal, SBEA IPMC) and has excellent training activity with four postdoctoral and two PhD past students who all contributed to published or submitted articles.

The quality and originality of the research is evidenced by its excellent publication record with 28 original articles in very high-profile journals (Lancet Neurology, Nat. Commun., J. Clin. Invest.) as well as excellent journals of pharmacology (e.g. Neuropharmacology, Br. J. Pharmacol.) and neuroscience (e.g. Mol. Psychiatry, J. Neurosci., J. Neuroinflam., Frontiers in Neuroscience, Neurobiol. of Disease, PLoS Comp. Biol.). The team production also includes eight reviews, among which one in a very high-profile journal (Physiological Reviews), and one book chapter. One team member also contributed two open source softwares (Sasdi, Vasd).

In addition, the team contributed to the dissemination of knowledge towards the general public through actions via the associations of patients (conferences, consultancy) or through actions towards schools.

Weaknesses and risks linked to the context

Funding relies essentially on the team leader which may represent a risk in a very competitive context..

No patents or declarations of invention are mentioned, and interactions with pharmaceutical companies remain limited.

All high-profile presentations were performed by the team leader, and most of the PhD students are officially mentored by the team leader, which may somehow hinder the progression of the other permanent researchers. One PhD student has been mentored by S. Cestèle (S.Dhifallah, PhD obtained in May 2020) during the evaluated period and one PhD student has been mentored by I. Léna (W. Marcantonio) with a PhD obtained in March 2023.

The research topics have enlarged in part through collaborative projects, but this may become a risk given the human resources of the team.

RECOMMENDATIONS TO THE TEAM

The research interests of the team being in strong connection with human pathologies, the team could consider strengthening translational aspects and entering pre-maturation programs.

The international recognition of the team leader being established, further strengthening the opportunity of career development for all permanent team members is recommended through fostering senior authorship, invited lectures, PhD mentoring, editorial activities and/or involvement in research management.

Team 17: Non coding genome & lung disorders

Name of the supervisor: Dr Bernard Mari

THEMES OF THE TEAM

The team focuses on the function of the non-coding genome and its potential application on human health, especially in lung diseases. They develop specific tools for loss- and gain-of-function approaches coupled with single-cell RNA-seq and various therapeutic approaches using antisense oligonucleotides (ASOs). Four main axes were covered since the creation of the team in 2018, i) ncRNAs as key regulators of the hypoxic response, ii) miRNAs as therapeutic targets in fibrotic diseases, iii) involvement of non-coding RNAs in wide aspects of physiological and pathological conditions, iv) application of functional genomics approaches regarding lung pathophysiology.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The committee of experts recommends to consider integrating additional types of data (i.e., epigenetic changes).
This recommendation has been addressed.

There are little European projects and funding. European and international recognition of projects and activities are not in line with the potential of the team.
Not addressed yet, with no European funding.

Efforts to attract and include more postdocs should be made.
Would need a further push.

Studies based on the investigation of human biological resources should be optimised (i.e., epigenetic and genomic studies, …). Use of human biological resources should be better optimised.
Not addressed.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	1
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	2
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)	0
Subtotal permanent personnel in active employment	**7**
Non-permanent teacher-researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	1
Post-docs	0
PhD Students	5
Subtotal non-permanent personnel	**6**
Total	**13**

EVALUATION

Overall assessment of the team

The team has an excellent to outstanding scientific production with fourteen original articles and five reviews (Oncogene 2019, Embo Mol. Med 2021). The visibility and attractiveness are excellent to outstanding with high levels of funding (1700 k€ and private partnerships), memberships to scientific societies (SFBBM, ERS), awards (Médaille de bronze CNRS, 2019), organisation and invitations to meetings (multiple facets of RNA, speaker at Keystone 2019). The non-academic activities are excellent to outstanding (2 patents, interviews in press and TV media).

Strengths and possibilities linked to the context

The visibility and attractiveness is excellent to outstanding and exemplified by high levels of fund raisings capacities over the period (1700 k€, with 1 ANRJC, 3 ARC, 1 grant from Agence Innovation Défense and several private-public partnerships, such as SATT-Sud Est, Galderma, Boehringer Ingelheim). Team members and the PIs are part of different scientific societies ('Société de Pneumologie de Langue Française' – SPLF –, 'Société française de Biochimie et Biologie Moléculaire' – SFBBM –, European Respiratory Society' – ERS) and journal editorial boards (PLoS One, Molecular Therapy-Oncolytics). One member of the team was awarded by national prizes from CNRS and passed his HDR (Médaille de bronze 2019, Scientific Excellence 2020). One post doc of the team got a permanent position at the CNRS in 2021. The team has excellent activities in organizing national and international meetings (Journées de Recherche Respiratoire, 2016, 2019, 2021 ; « The multiple facets of RNA in development and in disease ») and got numerous invitations in different national and international meetings for talks (Exiqon non-coding RNA workshop 2016; Keystone Meeting on Long Non-Coding RNAs 2019, ERS international congress 2017). The team leader is co-heading the Crispr-screening platform (cancéropôle Paca).

The team has an excellent to outstanding scientific production with a total of fourteen original articles and five reviews in key authorship position (over 53 publications in total) with important publications in their field (Oncogene 2019, AJRCCM 2019, Embo Mol. Med 2021).

The non-academic activities are excellent to outstanding with two patents (EP17811233A1, EP21305325.9), private-public partnerships (see above), and several interviews in different press and TV media (CNRS actualités ; Nice-Matin ; Cancéropôle Paca ; Université Côte d'Azur).

Weaknesses and risks linked to the context

Two weaknesses were identified first in the ratio of original papers versus total papers and second in the number of PhD vs postdoc. The risk would be the dilution of the resources towards collaborative works at the expense of main original topics of the team, in addition to the loss of renewal of expertise by the absence of postdocs.

RECOMMENDATIONS TO THE TEAM

The recommendation would be to limit collaborations to those really associated with the main topics of the team and put effort in recruiting international postdocs by increasing the visibility of the team members in different international meetings.

Team 18: Physiopathology of Neuronal Circuits and Behaviour

Name of the supervisor: Dr Hélène Marie & Jacques Barik

THEMES OF THE TEAM

The team is focusing on the characterisation of the specific sets of extrinsic and intrinsic factors inducing synaptic plastic changes and excitation/inhibition balance in learning and memory in rodents. They also analyse how these factors and balances are modified in various pathological conditions such as Alzheimer's disease, depressive disorders, anxiety and drug addiction.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

In comparison to the previous period (and according to previous Hcéres report), the team is clearly on an impressive dynamic curve: They have published twice more papers in the 2016-2021 period and in much more visible journals (e.g. eLife, Cell Reports, Nature Communications, Molecular Psychiatry, Science Advances). Team members clearly put a lot of efforts to successfully respond in full to the previous recommendations.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	1
Lecturer and associate lecturer	2
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	1
Subtotal permanent personnel in active employment	**6**
Non-permanent teacher-researchers, researchers and associates	3
Non-permanent research supporting personnel (PAR)	3
Post-docs	0
PhD Students	4
Subtotal non-permanent personnel	**10**
Total	**16**

EVALUATION

Overall assessment of the team

The team performs an impressive in-depth characterisation of synaptic phenomena for learning in control and pathological conditions. Team members (5 HDR) have an excellent to outstanding academic supervising activity since all PhDs and postdocs have regular first-authors publications. The team is on a very impressive dynamic curve and despite a heavy involvement of half of its members in academic duties, they carry out exciting research projects as illustrated by excellent to outstanding publications. The Team participation to outreach activities is excellent.

Strengths and possibilities linked to the context

The team is a very well established at IPMC with tight interactions with other teams of the unit. The research lines of the team address fundamental questions on plasticity changes related to various learning situations in control and pathological conditions. The team also incorporates computational modelling as a trans-disciplinary approach for in-depth analysis of their data and the generation of models to perform analytical exploration of plasticity. This point illustrates the proactive dynamics of the team.

During the 2016-2021 time period, team members were invited to give talks (33) mostly at a national level. Importantly, they have been involved also in organizing symposia and meetings. The team was labelled by the FRM, obtained a bronze medal from the CNRS and a nomination at the Institut Universitaire de France. The team has an outstanding level of fund rising since they have gathered vingt grants (total: 3.35 M€) and were coordinator for most of them (total of 2,257 M€). This includes two EU grants (JPND, FLAG-ERA JTC2019), five ANR (4 coordinator), six grants with patient associations/Fondations (all in coord; Fondation Alzheimer FRM, FRC, Inca, Fondation Vaincre Alzheimer, Association France Alzheimer) and local grants (Labex, Idex). Team members are involved in editorial boards (Neuropharmacol, Front Cell Neurosci, Front Syn Neurosci) and national and international evaluation/expertise panels (Hcéres, Inserm, CNRS, ANR ; ERC, DFG, Instituto Pasteur, Israel Science Fondation) and patient associations/fondations (Fondation Vaincre Alzheimer, Alzheimer Association-USA). The team doubled the number of permanent members (from 3 to 6, including 5 HDR), when compared to the previous period.

The number of original publications (23) in highly visible journals reflects a regular activity at an excellent to outstanding level. Twelve of these papers have a member of the team as first, last and/or corresponding author. Several (4) papers report on collaborations with IPMC teams. It should be noted that team members have developed over the years impressive international collaborative networks illustrated by numerous papers involving leading teams in their domain.

Team members are associate professors at the Université Côte d'Azur with heavy teaching duties and responsibilities such as the coordination of two new Master programs ('*Parcours Neurosciences Cellulaires et Intégrées*' and Mod4NeuCog Modeling for Neuronal and Cognitive Systems). In addition, the team members organise a training workshop 'Neuro-electrophysiology: from patch-clamp to in vivo recordings'. It is important to note that despites their strong dedication in academic duties, team members conduct outstandingly successful research projects from in vitro to in vivo with state-of-the art techniques (e.g. behavioural tasks, optogenetics, in vitro and in vivo electrophysiology).

Weaknesses and risks linked to the context

To gain even more visibility, team members should produce some review articles and/or book chapters.

RECOMMENDATIONS TO THE TEAM

The team should greatly benefit of more visible review articles.

Otherwise, the team is on an excellent and impressive dynamic curve, and their deep involvement in fundamental research and heavy academic duties should be encouraged and acknowledged.

Team 19: Sumoylation in neuronal function and dysfunction

Name of the supervisor: Dr Stéphane Martin

THEMES OF THE TEAM

The team investigates the regulation and functions of the Sumoylation process in neurons and neuronal synapses. The research performed aimed to analyse the impact of Sumoylation in the brain by focusing in parallel on the spatiotemporal regulation of the Sumoylation system and on the functional characterisation of newly identified neuronal/synaptic SUMO substrates.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous evaluation recommended not to engage in over-ambitious projects and to focus on a few interesting proteins and study the variation of their Sumoylation during development, to increase the team's size by getting new fundings, to establish contacts with industry when it will be relevant, to be more involved in teaching to attract students.

Considering the size of the team and the level of publications, the group has well managed its projects. It has focused on the analysis of the effect of Sumoylation of FMRP. Two national grants were obtained during the period, and three PhD students and one postdoc were recruited. Collaboration contracts were initiated with two start-ups.

WORKFORCE OF THE TEAM

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

EVALUATION

Overall assessment of the team

Considering the small size of the group, the production is excellent with four publications in primary journals (Nature Com 2018 & 2021, Molecular Psychiatry 2020, Cellular and Molecular Life Sciences 2019) with group members who were leaders in the corresponding studies, three reviews and six collaborative publications. The group has an excellent international visibility and is involved in three international and several national collaborations with well-renowned groups. The team has been successful in obtaining national funding. The Team participation to outreach activities is excellent (Brain awareness week, fête de la science).

Strengths and possibilities linked to the context

This is a relatively small team composed of two permanent members, three PhD students and one postdoc. The visibility of the group is excellent with three reviews and international collaborations. The team has been successful to obtain national grants in 2016 and 2021. During the period, group members supervised three PhD students and one postdoc. Each student published as first author and the postdoc published her work as co-first author. The team has established several collaborations at national and international levels with well-renowned groups leading to six collaborative publications.

Using a number of state-of-the-art imaging techniques and proteomics, the group reported that the Sumoylation process is regulated in a development and activity-dependent manner in the mammalian brain and critical to the formation of a functional neuronal network. During the period, they have shown that the Fragile X Mental Retardation Protein (FMRP) is modified in an activity-dependent manner by Sumoylation leading to the elimination and maturation of dendritic spines, adding an additional layer of complexity in the physiological regulation of FMRP in the brain. They also characterised the molecular, architectural and synaptic defects in the hippocampus of mutant experimental in vivo model affected for the Sumoylation of FMRP, as well as the associated synaptic plasticity impairment. In another study, they revealed that the synaptic balance between Sumoylation and deSumoylation is maintained by the activation of metabotropic mGlu5 receptors. Finally, the group achieved the first cartography of Sumoylation at the mammalian synapse. They identified about 800 synaptic SUMO substrates, many of them unknown until now, and defined an exhaustive list of new SUMO targets that are modified during the synaptogenesis period. Altogether this led to an excellent scientific production, with five main publications including Nature Com 2018 & 2021, Molecular Psychiatry 2020, Cellular and Molecular Life Sciences 2019.

The team is actively involved in the dissemination of knowledge to the greater public through its participation to several programs (Brain awareness week, fête de la science).

Weaknesses and risks linked to the context

The size of the group is small.

RECOMMENDATIONS TO THE TEAM

The team needs to get additional funding to increase its size.

Considering the size of the team but the potential offered by the identification of many endogenous synaptic SUMO-modified proteins in the mammalian brain, the team should be careful to identify strategic projects achievable by a small research group.

The international visibility of the team should be reinforced by the participation to international conferences.

The team is encouraged to continue its efforts to strengthen the innovation and valorisation aspects.

Team 20: Genomics & evolution in neuro-endocrinology (GENE)

Name of the supervisor: Dr Jean-Louis Nahon

THEMES OF THE TEAM

The team addresses questions related to the mechanisms set up at the level of a meal in a physiological situation or in neuro-inflammatory activation. It has explored how the modulation of neuronal activity has consequences for the regulation of energy homeostasis, including neuro-immunological mechanisms modulating appetite and body weight. The team is also interested in evolution. The team has focused on G – protein-coupled hMCHR2 protein, which is present in fish and primates, but not functional in rodents. They did a brain mapping and functional characterisation of the hMCHR2 receptor in a 'humanised' model.
The team also performed a comparative study of the structure and expression of 'primate-specific' PMCHL1/L2 genes in Macaques and in cellular models.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

· *Consolidated in term of human resources.*
Since 2020, recruitment of engineers and technicians, three postdocs in 2022, and arrival of a permanent researcher.

· *Improve the reputation of the team at the international level.*
The team has improved its international visibility and involvement in international training programs thanks to the Capes-Cofecub contract (Sao Paulo University, Brazil). A research Collaboration Agreement CNRS/University of Copenhagen, Denmark (DNK) has also been established (NNFCBMR, Copenhagen, DNK).

· *Improve recruitment of PhD students.*
Three PhD students have been recruited during the period.

· *Three objectives might be too large.*
The team has continued to follow three objectives.

· *Stronger interactions with the social, economic environment, as well as outreach activity.*
The team was strongly involved in the organisation of the 'Brain Week', an international event that gathered researchers and general public, which was extremely successful. It has also contributed to the Science Festival.
No industrial partnership has been established, since the team has chosen to focus on fundamental research.

WORKFORCE OF THE TEAM

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

EVALUATION

Overall assessment of the team

The production of scientific publications is very good to excellent with seventeen papers (14 original articles, 3 with IPMC, most in highly reputed journals – Embo Rep, Cell Rep… –, 5 in leading positions). Attractiveness is excellent with three PhD students (2 defended in 2019 and one co-supervised with Team 15) and a newly recruited DR2 CNRS. Funding is excellent, with coordination of nine out of ten projects. International collaborations supported by international grants demonstrated an excellent visibility. Excellent contributions to dissemination of scientific knowledge to the general public/institutional decision-makers/the media (Brain Week, Science Festival). The reputation is also excellent with several prizes and awards. There is also an outstanding investment in national and international responsibilities.

Strengths and possibilities linked to the context

Considering the human resources available for research over the whole period, the production rate was very good to excellent. The team has published regularly, and the majority in journals with high international visibility (Embo Rep 2016, Cell Rep 2020, Glia 2021, eLife 2016…). The literature review work on MCH and its receptors is regularly published in the best journal in the field, i.e., British Journal of Pharmacology results in very high citation rates.

Several articles reflect intense collaboration at the national and international level (e.g. Brazil: 4 articles, 7 communications at international conferences).

The training of PhD students looks excellent since they all co-authored publications.

The success rate for funding is excellent (three ANR contracts, one Itmo Cancer contract, two international contracts – Uca grant in collaboration with the Université Laval, Québec Canada, Research Collaboration Agreement CNRS-Univ Copenhagen – and Uca funding – PsyCoMed, NutriNeuro – will contribute to maintaining and even develop team activity with the recruitment of postdocs and engineers.

The attractiveness of the team is confirmed by the arrival of a talented newly recruited DR2 CNRS. He opens strong opportunities to develop new collaborations and will contribute to reinforce the team after the retirement of the current PI.

The involvement of the team in dissemination of science is remarkable as exemplified by the organisation of the Brain Awareness Week in 2018, which was a very important event gathering more than 7000 people as well general public as experts of the field. Moreover, the team was involved in the co-direction of the 'Primate Biobank' that consists in acquiring, validating, studying and distributing a collection of non-human primates and specimen of these organisms – tissue fragments, nucleic acids (DNA, RNA), proteins, etc. – .

A key point that should be acknowledged is the outstanding investment in responsibilities of all the permanent team members. – Presidence of Scientific Councils (Labex Signalife, EUR LIFE, etc.), management of CNRS Units (SdP UPS 846 2012-2017, IPMC UMR7275 since 2018). This is also made at the international level with the development of international programs (Chairman IUPHAR 'MCH/MCH receptors', USA; Program Capes/Cofecub France-Brazil; RCA NovoNordisk, Denmark).

Weaknesses and risks linked to the context

The translational activity has decreased in the last period.

The three researchers of the team were heavily involved in research administration (Scientific Councils/Expertise Committees/CSS Inserm), which is an excellent point in terms of visibility but might affect the team's productivity.

RECOMMENDATIONS TO THE TEAM

The valuable and unique expertise of the team should be preserved and transferred to the next group leader.

The objectives should be in proportion to the available human resources. Funding applications should be maintained to guarantee these human resources.

CONDUCT OF THE INTERVIEWS

Dates

Start: 23 January 2023, 8:45 a.m.

End: 24 January 2023, 4:45 p.m.

Interview conducted: on-site

INTERVIEW SCHEDULE

IPMC
Program of the visit
January 23-24, 2023

DAY 1, Monday 23 January

8:45 – 9:00 Preliminary meeting of the expert committee (closed hearing)
Attending: expert committee, Scientific Officer (SO) (MJ Stasia)

9:00 – 9:15 Presentation of the Hcéres evaluation to the unit (Marie José Stasia, SO)
Attending: expert committee, SO, representatives of institutions and all unit members

9:15 – 10:30 Presentation of the research unit by the unit director/Deputy director (including 30 min questions)
Attending: expert committee, SO, representatives of institutions and all unit members

10:30 – 10:45 Break

10:45 – 11:45 Parallel meetings (3 Expert groups)
- Meeting with technical and administrative personnel (in French)
Attending: Technicians, Engineers, Administrative staff, sub-committee 1 of expert committee, SO (Yacine Graba)
- Meeting with thesis students and postdocs
Attending: PhD students and postdocs, sub-committee 2 of expert committee, SO (Marie José Stasia)
- Meeting with researchers and professors
Attending: Researchers except group leaders, sub-committee 3 of expert committee, SO (Ina Attrée)

11:45 – 1:30 p.m. Lunch

1:30 p.m. – 2:30 p.m. Committee debrief (closed hearing: synthesis of staff meetings and first 'content' draft of unit evaluation)

2:30 p.m.-5 p.m. Parallel scientific team presentations (2 sub-committees/5 teams)
30 min/team (15 min presentation + 10 min questions + 5 min debriefing of the committee)
Attending: Team members, expert committee, SO, director of Unit, representatives of Institutions

Sub-committee 1
Team 1: Dynamics of lipid membranes and protein coats (B. Antonny)

Team 2: Physiological genomics of the eukaryotes (P. Barbry)
Team 3: RNA metabolism and neurodevelopmental disorders (B. Bardoni)
Team 4: Immune regulations at mucocutaneous surfaces (V. Braud and F. Anjuère)
Team 5: Molecular & cellular biology of normal & pathological cerebral aging (F. Checler)

Sub-committee 2
Team 11: Molecular and Integrative Mechanobiology (E. Honoré) (visioconférence)
Team 7: Arf proteins, cell morphology & membrane transport (M. Franco and F. Luton)
Team 9: Metabolism and functions of membrane lipids – (ATIP/Avenir) (T. Harayama)
Team 10: Neuropeptides, brain diseases and therapeutics (C. Heurteaux and J. Mazella)
Team 13: Molecular physiopathology of phospholipases A2 & their mediators (G. Lambeau)

5 p.m. – 6 p.m. Sub-Committee debrief (closed hearing: synthesis of team evaluations and continued writing of the draft of unit evaluation)

8 p.m. Diner

DAY 2, Tuesday 24 January

8:30-11:00 Parallel scientific team presentations (2 sub-committees/5 teams)
30 min/team (15 min presentation + 10 min questions + 5 min debriefing of the committee)
Attending: Team members, expert committee, SO, director of Unit, representatives of Institutions

Sub-committee 1
Team 6: Lipid transport in health & diseases (G. Drin)
Team 8: Immune system, brain and peripheral nerves (Pr N. Glaichenhaus)
Team 12: Mechanisms of gene regulation in physiopathology (E. Lalli)
Team 17: Non coding genome & lung disorders (Dr B. Mari)
Team 20: Genomics & evolution in neuro-endocrinology (GENE) (Jean-Louis Nahon)

Sub-committee 2
Team 14: Molecular physiology and pathophysiology of ion channels (F. Lesage)
Team 15: Ion channels and pain (E. Lingueglia and E. Deval)
Team 16: Pathophysiology of voltage-gated Na+ channels and neuronal excitability (M. Mantegazza)
Team 18: Physiopathology of Neuronal Circuits and Behaviour (H. Marie and J. Barik)
Team 19: Sumoylation in neuronal function and dysfunction (Stéphane Martin)

11:00 – 12:00 Sub-Committee debrief (closed hearing: synthesis of team evaluations and continued writing of the draft of unit evaluation)

12:00 – 12:45 Meeting with the representatives of CNRS and University CA
Attending: Expert committee, SO, representatives of Institutions

12:45 – 1:45 p.m. Lunch

1:45 p.m. – 2:45 p.m. Meeting with the head of the unit/deputy director (closed hearing: synthesis of team evaluations)
Attending: Unit director, expert committee, SO

2:45 p.m.-4:45 p.m. Final committee deliberations (closed hearing)
Attending: expert committee, Scientific Officer

GENERAL OBSERVATIONS OF THE SUPERVISORS

Présidence et services centraux

Direction de la Recherche, de la Valorisation et de l'Innovation
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Nice, le 10 juin 2023

à l'attention du Haut Conseil à l'Evaluation de la Recherche et de l'Enseignement Supérieur

Objet : **Observations de portée générale**

Unité : UMR7275

Team 3 / Barbara Bardoni

I thank the HCERES committee for the time they spent to evaluate our report and for their comments and suggestions.
As suggested by this committee, it will certainly be a priority for us to increase the workforce of the team especially with the recruitment of permanent staff.
I would like to underline that in this sense the dynamics have been positive during the last 2 years:
Since November 2022, Dr. Carole Gwizdek CRCN CNRS has joined the team bringing the number of HDRs to 3 (in addition to Dr. Capovilla and myself).
Since January 2022, Dr. Sébastien Delhaye has been recruited as a post-doc.
Since October 2022 Dr. Alessandra Tempio has been recruited as a post-doc. She had a secondment in our team in 2021 during her PhD at the University of Catania.
Starting from June 2023, Dr. Aurore Thomazeau will integrate the team. She is a senior post-doc who has been working at McGill University (Montréal, Canada) in the Sjöström laboratory since 2019. Since 2021 she has been supported by an MSCA - Global action fellowship to develop a collaborative project between our and the Canadian laboratories. Aurore Thomazeau is expected to obtain a HDR during 2024 and to apply for a CNRS position for CRCN and MC for UCA.

Team 6 / Guillaume DRIN

Weaknesses and risks linked to the context
The main weakness is the human resources of the team, which limits in particular the capacity to train PhD students (only 1 HDR). No recruitment on permanent position has happened during the period.
An identified threat is the capacity to secure proper funding resources. Consequently, the risk is to lose the unique expertise and international visibility by being more involved in collaborative projects than leading their own views. This is the risky counterpart of the opportunity.
An Inserm CRCN (with HDR) will join the lab within this year (see below), which will re-inforce our human resources. As underlined by the committee, we manage to have an excellent/outstanding scientific production despite our small size (2 FTEs); to sustain this effort, we hope to have a renewed support of the IPMC to have the equivalent of a full-time permanent IE in the team. We constantly apply for grants dedicated to our core topic. Yet, it is noteworthy that within projects as collaborator, notably ANR PRCs, we also have the opportunities to lead studies, not necessarily on lipid transfer mechanisms, and to publish as corresponding author (e.g., Milanini et al., JBC, 2022, ANR COCON; soon with ANR REMIND). This allows us to keep developing our more general yet recognized expertise in biochemistry/biophysics and protein/membrane interaction, while developing other themes in the team, which might represent a chance in the future.
Recommandations to the team
- In terms of attractiveness, the quality of the scientific environment should make it possible to attract brilliant young researchers, doctoral students and post-doctoral students, particularly from abroad.
- A common scientific strategy linking fundamental research and translational research could make it possible to secure project financing capacities and to envisage recruitment (clinicians, engineers, etc.).
Dr. Mounia Louet, an Inserm CRCN previously at C3M in Nice, attracted by our thematic, will join the lab at the end of the year 2023 to work on the interplays between VAMP-7 dependent-vesicular trafficking, sterol transfer and steroidogenesis. She has a strong background in the mechanisms controlling steroid hormone production and signaling and their dysfunction in metabolic disorders and malignancies in humans, as well as their impact on sexual dimorphic traits. Therefore, her expertise is very complementary to ours, which provides opportunities to develop project at the crossroad between fundamental and translational research.

Team 16 / Massimo Mantegazza

Overall, the strengths highlighted in the "Strengths and possibilities linked to the context" section have been attenuated in the other sections of the evaluation, including the number and level of the publications and the funding obtained. In particular, the "weaknesses" and "recommendations" sections of the evaluation underestimate the involvement of the other permanent team members: they are involved in research management, PhD mentoring, editorial activities (e.g. reviewing), invited lectures, and they all have senior authorships. Notably, some of these points have been correctly listed in the "Strengths" section. All the members participate to the efforts and contribute to set strategy and tactic via regular meetings of the permanent members. During these meeting we discuss also about opportunity of career development for all team members.

Florian Lesage,
directeur de l'IPMC

Présidence et services centraux

UNIVERSITÉ CÔTE D'AZUR | cnrs

Nice, le 17 juillet 2023

Direction de la Recherche, de la Valorisation et de l'Innovation
Mme Johanna ZERMATI
Directrice

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à l'attention du Haut Conseil à l'Evaluation de la Recherche et de l'Enseignement Supérieur

Affaire suivie par :
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Gestionnaire

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Objet : **Observations de portée générale**

Veuillez trouver ci-après les observations de portée générale d'Université Côte d'Azur concernant l'unité **DER-PUR230023179** - **IPMC - Institut de pharmacologie moléculaire et cellulaire**.

Université Côte d'Azur would like to thank the entire HCERES Committee for the consistent and quality work in analyzing and evaluating the activities of the IPMC institute. The Committee's assessments and recommendations on the various areas of assessment are very useful for positioning the unit's activities and providing elements on which to rely to consolidate the unit's forward-looking vision.

The institution has no comments to make on the Committee's report.

UNIVERSITÉ CÔTE D'AZUR 27.07.2019

Pour le Président d'Université Côte d'Azur
et par délégation,
Le Vice-Président Recherche et Innovation

Noël DIMARCQ

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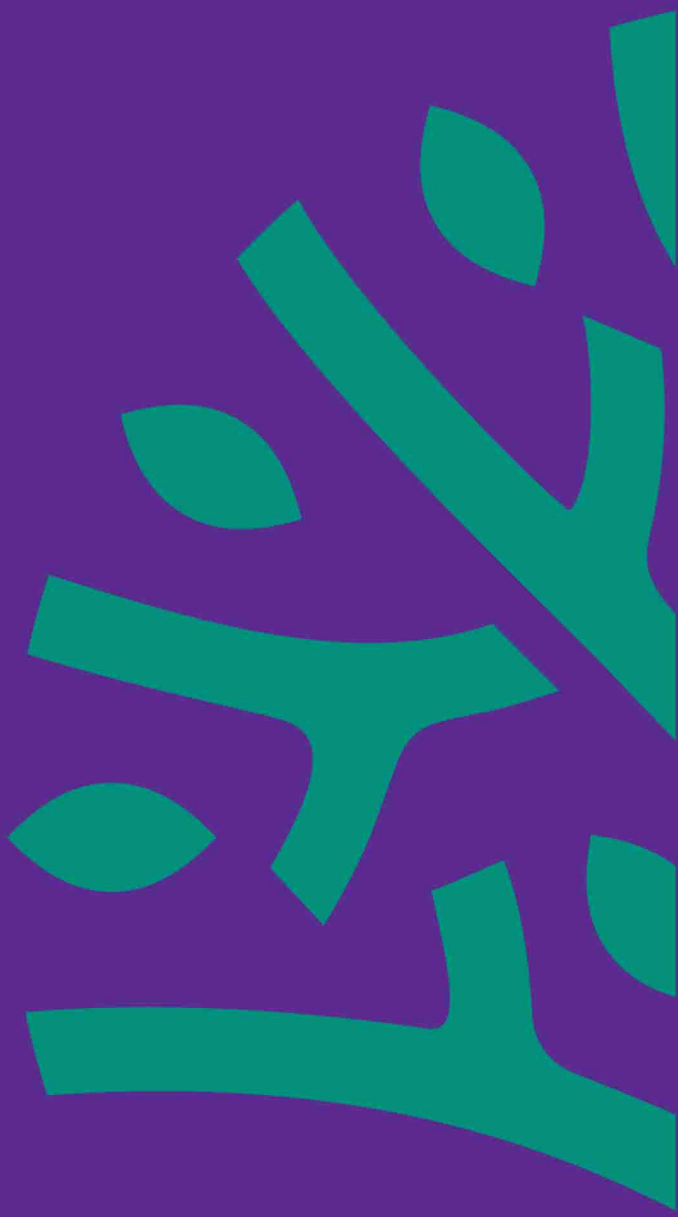

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