

EVALUATION REPORT OF THE UNIT
IFM - Institut du fer à moulin

UNDER THE SUPERVISION OF THE
FOLLOWING ESTABLISHMENTS AND
ORGANISMS:

Sorbonne Université,
Institut national de la santé et de la recherche
médicale, Inserm

EVALUATION CAMPAIGN 2023-2024
GROUP D

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In the name of the expert committee¹ :

Ellouise Anderson Leadbeater, Chairwoman of the committee

For the Hcéres² :

Stéphane Le Bouler, acting president

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

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

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

MEMBERS OF THE EXPERT COMMITTEE

Chairperson:

Ms Ellouise Anderson Leadbeater, Royal Holloway University of London
Royaume-Uni

Experts:

Ms Carine Ali, Université de Normandie, Caen (CNU representative)
Ms Elena Avignone, Université de Bordeaux, Bordeaux
Mr Luc Dupuis, Institut de la Santé et de la recherche Médicale - Inserm
(CSS4 Inserm representative)
Mr Etienne Guillaud, Centre national de la recherche scientifique –
CNRS, Bordeaux (PAR representative)
Ms Fabienne Pituello-Berniere, CNRS - Centre national de la recherche
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Milan, Italie

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Mr Giovanni Stevanin, Inserm - Institut national de la santé et de la recherche
médicale, Bordeaux

REPRESENTATIVE(S) OF SUPERVISING INSTITUTIONS AND BODIES

Not applicable (evaluation performed on files)

CHARACTERISATION OF THE UNIT

- Name: Institut du Fer à Moulin
- Acronym: IFM
- Label and number: UMR-S 1270
- Composition of the executive team: Fiona Francis (co-dir: Jean-Christophe Poncer)

SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement
SVE5 Neurosciences et troubles du système nerveux

THEMES OF THE UNIT

The IFM teams share common interests with convergence to several main research themes, notably 'brain development' and 'plasticity'. Established in 2007 as a newly formed research institute dedicated to molecular and cellular neuroscience, IFM has since expanded to accommodate groups interested in technologies ranging from the study of neural stem cells and cell engineering to in vivo electrophysiological recordings during rodent behaviour.

One primary focus lies within developmental neuroscience. Numerous groups investigate neurodevelopment and its disruptions leading to neurodevelopmental disorders such as learning disorders, autism spectrum disorders (ASD), depression, epilepsy, and motor neuron diseases.

The second major research axis at IFM concentrates on neurotransmission and plasticity in the adult nervous system, along with their pathological and pharmacological alterations.

Areas of expertise encompass genetics, molecular biology, cellular biology, biochemistry, neuroanatomy, electrophysiology, and behavioural studies.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The IFM stands as a distinguished research institute affiliated with Inserm and Sorbonne Université (SU). Nestled within the expansive Paris Hospitals Administration (APHP) complex, alongside the Central Pharmacy of Paris Hospitals (Agence générale des équipements et produits de santé) and the School of Surgery, its strategic location fosters collaboration and synergy. Adjacent to the renowned Pitié-Salpêtrière hospital and the SU Pierre et Marie Curie main campus (formerly known as Jussieu's campus), and close to the well-known Ecole Normale Supérieure (ENS), Curie Institute and École Supérieure de Physique et de Chimie Industrielles de Paris (ESPCI), IFM has been a beacon of scientific inquiry since its inception in 1968.

Initially spanning approximately 2500 m², the IFM building has been under the stewardship of Inserm, accommodating various research units across diverse fields. Its evolution traces back to 1996 when the Intracellular Signalling unit (U440), under the leadership of André Sobel, laid the foundation for a thematic vision culminating in the 'Institut du Fer à Moulin'. This vision gained momentum in 2000 with the establishment of Unit 536, 'Signalling and plasticity in the nervous system'. This pivotal moment witnessed a convergence of scientific endeavours, fostering cross-disciplinary exchanges and potential synergies.

The collaborative ethos of IFM extended beyond mere coexistence; shared resources, personnel, and expertise became the norm. Regular joint lab meetings, seminars, and communal management of supplies facilitated a dynamic research environment. Recognising the need for expansion, concerted efforts in 2006 led to the renovation of additional space, supported by funding from Inserm, the Ile-de-France region, and the Bettencourt-Schueller Foundation. Three additional teams from the Pitié-Salpêtrière joined the project and proposed to form together a single 'Research Institute' in the field of Neuroscience, the 'Institut du Fer à Moulin'. In end 2022, the IFM was made up of a staff of 90–110 people, including bachelor and master students. This included 43 permanent staff (19 technical staff and 24 scientists) employed by Inserm, the CNRS and SU. The remaining staff consists of post-docs and PhD students, as well as short-term interns and visiting scientists. There are eight research teams (3–14 people) and one Translational Program group (2 people). There are administrative and logistical support staff. There are three platforms, and common equipment is regrouped in a further four technical facilities.

RESEARCH ENVIRONMENT OF THE UNIT

The IFM is a research institute affiliated with Inserm and Sorbonne Université (SU). The visibility of IFM received a significant boost with the establishment in 2008, under the coordination of the former director of IFM, of the Paris School of Neuroscience (ENP), a highly competitive regional network of excellence. The ENP was taken up finally

by the Fondation Sorbonne Université under the name 'Fondation des Neurosciences de Paris', and now supports and inspires new programs aimed at attracting outstanding international students through its collaborations with the new DIM C-BRAINS.

In 2011, IFM teams actively participated in a national competitive call for 'Laboratories of Excellence' (Labex Bio-Psy) network project application. Given that all IFM labs either partially or fully engage in topics related to mental illness, this presented an excellent opportunity to strengthen collaborations with clinicians and secure funding.

IFM has also played a pivotal role in driving the 'Neuroscience domaine d'intérêt majeur' projects (C-BRAINS), competitive networks funded by Région Ile-de-France (€12.5 million, 2022–2026) aimed at bringing together outstanding groups in the chosen domain. C-BRAINS was initiated by an IFM member who is now one of the three co-directors of this funded program.

Furthermore, several IFM groups are affiliated with the FHU Adapt project (Médecine de Précision en Addictologie et Psychiatrie) and are involved in the PEPR ProPsy project (Program Project in Precision Psychiatry), which received successful funding in 2022. Additionally, four groups are included in the Groupement d'Intérêt Scientifique 'Autisme & Troubles de Neurodéveloppement,' and six groups contributed to the IHU Institut du Cerveau de l'Enfant (ICE) project (submitted in November 2022).

The unit has easy access to many facilities in the ENS, ESPCI, and ICM units as well as within the SU campus.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	6
Directeurs de recherche et assimilés	8
Chargés de recherche et assimilés	8
Personnels d'appui à la recherche	19
Sous-total personnels permanents en activité	43
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	1
Post-doctorants	7
Doctorants	21
Sous-total personnels non permanents en activité	29
Total personnels	72

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

Nom de l'employeur	EC	C	PAR
INSERM	0	10	16
SORBONNE UNIVERSITÉ	8	0	3
AUTRES	0	6	0
Total personnels	8	16	19

GLOBAL ASSESSMENT

The Institut du Fer à Moulin carries out fundamental research into the development and plasticity of the nervous system. Positioned at the centre of Parisian neuroscience, it benefits from an **outstanding national and international reputation and high visibility**, which is all the more commendable given its relatively smaller size in comparison to several other Parisian institutes. The researchers of the IFM are exceptionally active in initiatives that both promote this visibility and justify their reputation, including the organisation of scientific meetings that attract international invitees. This is a unit with a deservedly **outstanding reputation**.

In terms of productivity, the Unit maintains an **excellent portfolio of outputs**, with 92 publications in lead positions (first/senior author) over the contract period, many in highly reputed journals (e.g. Cell Reports) and some at the top tier (e.g. Nature Communications). A further 53 co-authored articles include publications in Science and Nature Communications, among many others. An appropriate level of collaboration between teams is evidenced by the fact that 30 publications involve more than one IFM team and/or core facility. A broad range of approaches, from genetics and molecular neurobiology to functional research into neuron function and even behaviour, are encompassed within these outputs.

On a societal level, the IFM plays an active role in the national scientific community (leadership of the Society for Neuroscience) and in Europe (leadership of FENS and the Bio-psy labex), as well as in raising public awareness (participation in patient association meetings and national neuroscience events such as the Fête de la Science and Brain Week). In addition, interactions with industry (AtmSR, UCB, Axonis), collaborations with clinicians on neurodevelopmental pathologies and efforts to promote research (5 patents produced during the last contract) testify to the concrete impact of IFM research on society, despite its highly fundamental approach to research. Examples of main results include the molecular characterisation of two striatal neuron types [D1 and D2] (Nat Comm 2017), the role of Dlgap4 and Yif1b proteins in brain development (Brain 2020, Nature Comm 2022), the description of the anti-epileptic potential of molecules acting on the KCC2 channel (patent), the importance of the serotonin 2B receptor during development in mitigating adult neuroinflammation (Glia 2021) and the first production of spinal organoids (Development 2019).

IFM teams are well resourced financially, particularly in terms of competitive research grants (>100 contracts over the period) including (in France) nineteen ANR, of which 50% are as lead, and (in Europe) 6 JPND or Eranet Neuron (1/3 as leaders), but also through support through its supervisory bodies (Labex, Idex). Further secured funding is dedicated to its core equipment, and the IFM benefits from access to Labex BioPSy and DIM C-Brains.

The management and functioning of this Unit are exemplary, with clear attention paid to the career development of staff at all levels, to good practice in terms of Open Research, and to communication and transparency within the Unit. There are clear efforts to maintain an international friendly atmosphere, including specific efforts to welcome new researchers and promote collegial leadership. Historically, these have paid off in terms of attracting promising researchers with the ability to secure competitive funding (5 ATIP Avenir prior to the current period) and this trajectory continues (2 current ATIP Avenir). A high proportion of researchers (70% of postdocs, 20% of PhD students) are from outside France.

Despite its clear success, the IFM is facing a time of change, with the planned closure of the current building and the dispersal of the teams to multiple institutes, the majority destined to merge with the Neuroscience Paris Seine unit (NPS) and form the new NEURO-SU unit on the Pierre et Marie Curie Campus of Sorbonne University. This transition, though carefully planned, presents a challenge in terms of management and is likely to require careful communication and significant strategic efforts to maintain productivity despite disturbance and timescales that may be difficult to plan around.

DETAILED EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

There were no specific recommendations regarding criteria 1 (scientific production and activities) and three (scientific strategy and projects). This highlights the quality of IFM regarding these items, which has not decreased since then. For example, the number and quality of publications have been maintained. Most recommendations concerned the criterion 2 'the unit's organisation and life'.

The **first point** was to maintain the team spirit within the institute, which has been the case, even during the COVID19 pandemic: indeed, although access to the centre was then restricted, all efforts from the PIs and the Direction have been deployed to maintain as much interactions as possible. Most lab members showed their adherence to the institute, doing their best to run the lab. Such a cohesion has allowed for maintenance of some activities that are critical to the lab and scientific discussions. Otherwise, in house social and scientific exchanges are well considered (events, common rooms) and internal reorganisations (administrative and logistical services, core facilities) have been beneficial for all users.

The **second point** raised was to prepare a serene transition that considers the anticipated retirement of some PIs, the turnovers in teams, and more administrative issues regarding the future of the building. The IFM, via its SAB, has been proactive (and successful) in new competitive recruitments, having attracted two talented junior researchers, both laureates of the ATIP-Avenir grant who have been awarded a permanent researcher position (CRCN) at INSERM. This has allowed a fruitful turnover in the teams of the institute.

As for the risk regarding buildings, despite their constructive efforts, members of the IFM were dependent on institutional discussions.

The **third and fourth comments** related to communication in general within the institute, at several levels and for issues about science, strategy, finances, integration of new staff members. Following these comments, and taking advantage from its 'humane' size, the IFM has pursued or engaged many actions to ensure a high level of transparency. Importantly, information circulates appropriately, to ensure both the independency of each team and the IFM strategy at the same time. Also, exchanges occur in appropriate manners/meetings, ie upstream, between concerned people/representatives to adopt the best strategy, and downstream, to inform all members of the IFM, whatever their status. Information is provided via electronic means, during regular administrative meetings, team meetings, user's meetings (with the core facility scientific and operational staff, as well as support staff leaders or with the core facilities and other IFM technical groups), Research Centre Council meetings and General assembly meetings. Early career scientists are also encouraged to interact together and with PIs, regarding raw data, technical issues or ready-for-submission results.

B – EVALUATION AREAS

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

Assessment on the scientific objectives of the unit

The IFM, which is focused on understanding neurological and psychiatric disorders, collaborates extensively despite not directly engaging in clinical research. With ongoing projects, patent filings, industrial interactions, and public engagement efforts, the institute navigates challenges. The impending sale of its current Paris site poses limitations on future growth, prompting the dispersion of IFM groups. Despite this, the institute sustains a diverse, proactive, and collaborative community, fostering a communicative atmosphere. The relevance of the unit's objectives within the neuroscience research community is outstanding.

Assessment on the unit's resources

The eight constituent teams have 72 research staff, including 43 permanent ones (24 researchers and 19 technical staff, which is an excellent ratio for a unit that needs to maintain its technical expertise). The IFM consistently secures financial resources, including Labex and DIM local support, with ~100 contracts totalling ~€25m over the period, commendable for its size. Despite potential challenges from rising consumable prices, internal reflections and cost comparisons maintain all activities. Initiatives like Labex and DIM programs, promotion of emerging projects during the Covid pandemic, and plans to optimise lab space showcase the institute's resilience and strategic engagement. Despite potential challenges from the future move of IFM groups, the institute maintains excellent lab conditions. Overall the IFM resources are excellent to outstanding.

Assessment on the functioning of the unit

The IFM consistently follows Inserm and SU directives, ensuring diverse and fair recruitment. Proactive communication addresses potential anxieties related to the future move. Training demands, especially in animal experimentation, pose challenges, but initiatives for M2 student training periods alleviate the situation. IT practices and data security are actively managed, with update plans supported by Inserm and SU. The IFM prioritises environmental sustainability through recycling. Business continuity plans showcase the institute's excellent adaptability and rapid response to changing situations.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

Scientific objectives focused on studying nervous system development and plasticity in mammals align with Inserm and SU's biomedical research strategy. IFM enjoys an excellent working environment supported by supervisory authorities, evident in robust financial backing received from 2017–2022. Substantial individual grants from national and international sources (~ 25 M€ over the contract period) underscore financial strength. Interdisciplinary work fosters nascent collaboration in biophysics (new collaboration with ENS Ulm) and mathematics research (new collaboration with the University of the Cote d'Azur). Effective organisation provides a conducive environment for research groups with complementary expertise. Areas of expertise include genetics, molecular biology, cellular biology, biochemistry, neuroanatomy, electrophysiology, and behavioural studies, promoting synergistic interactions to generate novel diagnostic and therapeutic approaches, with projects ranging from molecular to systems and behavioural neuroscience.

IFM has received significant support from Inserm and Sorbonne University, leading to notable expansions in personnel. Inserm has provided funding for equipment and recruited two researchers, 4 technicians, and two administrative staff. Sorbonne University has increased financial support and facilitated collaborative initiatives. The IFM has successfully recruited two new junior groups and attracted a diverse cohort of PhD students and post-docs, enhancing its research capabilities and fostering an international atmosphere.

The IFM's organisational structure, including the Research Center Council, Principal Investigators Meeting, and Technical Staff, fosters communication and strategic decision-making. A welcoming environment for new members is established through a bilingual 'Welcome booklet' and various committees. Active participation in scientific advisory boards contributes to the IFM's visibility and reputation such as IBENS, ERA-NET Neuron, and Cortex-Labex.

Weaknesses and risks linked to the context

Potential vulnerability arises from the imminent sale of the current site by AP-HP, limiting future growth and prompting the dispersion of IFM groups. The excellent working environment faces a threat due to the impending change in location, impacting the institute's overall strategy and operations. Challenges may emerge in maintaining the institute's dynamic and collaborative atmosphere after the move of IFM groups. While the interdisciplinary approach is a strength, maintaining effective communication and information dissemination to all institute staff will be an ongoing challenge. While the IFM has maintained financial and logistical support, the turnover and renewal of technical personnel necessitate ongoing efforts for smooth operations.

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

Strengths and possibilities linked to the context

The IFM is highly competitive and receives significant funding from diverse funding sources e.g. ANR at the national level, Eranet Neuron at the European level). Among these, IFM coordinates approximately 50% of the ANR grants, and around 1/3 of European grants are coordinated by the IFM team. Financial support has increased over the mandate. Annual support from Inserm and SU is consistent, totalling €446,000. Additional state funding, including a young researcher and exceptional credits, has been substantial (€606,000 in 2022). Access to common facilities is charged to research groups at validated prices, ensuring financial sustainability of core facilities. Investments in stem cell/organoid research and in vivo recordings demonstrate the institute's commitment to emerging themes and teams.

Collaboration among IFM groups in grant applications, such as Labex BioPsy and C-BRAINS, showcases a collective effort to enhance research activities. Acquisition of funds for state-of-the-art imaging equipment (e.g. Zeiss Cell Discover, La Vision Lightsheet) strengthens IFM's capabilities, with complementary support from e.g. Région, Brain Research Federation, Inserm, and SU. Active involvement in research networks (FHU-Adapt, i-Bio, and ICE) demonstrates IFM's strong reputation.

IFM's infrastructure is well designed. Open laboratories enhance communication, with spaces tailored to diverse research needs, e.g. electrophysiology and cell culture. Recent renovations, particularly in the animal experimentation core facility, highlight IFM's commitment to maintaining and enhancing its infrastructure to meet evolving research needs.

Weaknesses and risks linked to the context

The dispersion of grant sources, while diverse and beneficial, may introduce complexities in managing and coordinating activities across various funding entities.

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

Strengths and possibilities linked to the context

IFM is dedicated to promoting fair research assessment, equity, and inclusion in neuroscience, exemplified by early adoption of the ALBA Declaration (<https://www.alba.network/declaration>). Rigorous recruitment processes, such as broad postdoc announcements and Master 2 internship assessments, underscore their commitment. Participation in global programs like ENP, i-Bio, and C-BRAINS attracts international students. IFM actively promotes gender equality through balanced team leadership and participation in gender committees. Yearly assessments, internal organisation, safety officers, anonymous questionnaires, and medical visits contribute to a comprehensive approach to well-being and safety. The small institute size enables responsive management and a commitment to external evaluations for continuous improvement.

Scientific asset protection involves a GMO (Genetically Modified Organism) register at the Research Ministry, and recent hires for regulatory oversight. Robust computer systems include roaming profiles, centralised storage, and external service provider (applicant tracking system, ATS) management for IT efficiency. Internal rules and a charter ensure secure information system access. Shared data storage with backup aligns with data security best practices.

Ethical procedures govern human samples and rodent experimentation, with ongoing efforts for authorisation and rigorous training, including a 'skills booklet'. Active participation in a CO2 emissions network highlights environmental responsibility.

Weaknesses and risks linked to the context

As far as Biological Sample Storage, although well-equipped, potential risks lie in centralised storage, requiring robust backup systems, especially considering past interruptions in backup procedures. Computer Systems: Dependency on an external service provider may present a risk if not managed effectively.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The IFM is outstanding in terms of its staff hosting policy and the care that it devotes to maintaining a collegiate, welcoming atmosphere. International staff are a high proportion of the workforce (1/5 of the team leaders and 77% of post-docs). The IFM has seen high levels of competition during recruitment events, and has attracted earlier-career team leaders with impressive scientific trajectories. Integration into the European research network is excellent and includes leadership of European consortia, with a strong reputation evidenced through prizes to individual researchers. There is potential for more EU funding, however.

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

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

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

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

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

The IFM is a highly attractive unit with commendable scientific standing that plays a role in building the local, national and European research landscape. This is evidenced through, for example, organisation of national conferences (NeuroFrance2017) and contributions to the scientific committee for international conferences (FENS 2022; including organising a satellite meeting). At a more local level, the IFM organises an annual colloquium which twice secured Labex support and attracts international invitees, alongside Parisian research exchange networks (e.g. Young Researcher Days).

IFM researchers also contribute to French and European research by presenting their own research at national (12) or international (32) conferences, and by organising symposia (e.g. Maroteaux Keystone symposium 2017). The IFM's work has been recognised with national prizes (e.g. Fondation Française pour la Recherche sur l'Epilepsie, twice), including those awarded to earlier-career researchers (e.g. NARSAD Young Investigator Awards). In the last mandate, IFM members participated in significant European projects and actions, such as the FP7 project for epilepsy research (DESIRE), including as Principal Investigators for several European Eragnet Neuron or JPND projects (n=2 of 6). Additionally, IFM members actively contributed to grant reviewing at the European level, showcasing their strong presence in European research forums and programs.

The unit is attractive due to the outstanding quality of its staff hosting policy. Care is taken to welcome new recruits, who undergo a comprehensive orientation process, receiving information via a welcome booklet and signing various charters. They tour the facility and receive specialised training in areas such as microscope usage and facility procedures. Health and safety training is mandatory, and individual team members also contribute to their integration by sharing expertise. New staff are also introduced during weekly 'Progress Report' sessions, and invited to give seminars. It is clear that the small size of the institute contributes to its welcoming nature.

The unit's attractiveness is also evidenced through its success in recruitment. Both of the newest recruits are recipients of ATIP-Avenir, and one was recruited through a highly competitive process that attracted high numbers of applications. A relatively high proportion of the scientific staff are international, particularly postdocs (77%). The unit attracts visiting researchers, from professors (USA) to PhD students (France; Portugal; plus rotation projects) and participates in exchange schemes (e.g. IBRO). To promote their international hosting, internal communications among scientists are in English.

IFM teams consistently secure funding from national and international calls (~€25m total contracts over the contract period). Funding information is shared through weekly electronic newsletters, team leaders, and various online platforms. Each team independently pursues funding opportunities without restrictions, maintaining scientific autonomy. Team leaders and other researchers actively support younger researchers in their grant applications, particularly through internal peer review, fostering a collaborative and successful environment. This provision is outstanding. In addition, the support provided by the Labex BioPys and C-Brains DIM, both of which have involved IFM members in key leadership roles, renders the unit highly attractive.

Over the years, the IFM has acquired advanced equipment through collaborative efforts from multiple teams, funded by sources such as charities (FRC/Rotary Espoir en Tête), regional programs (DIM Cerveau et Pensée, DIM Biothérapies, DIM C-BRAINS), Labex Bio-Psy, and funding from Inserm and SU facilities networks. Major equipment is housed in core facilities for Cell and tissue imaging, Cell and tissue engineering and Rodent breeding and phenotyping, managed by dedicated staff as part of SU facilities networks (LUMIC for Imaging, RPPA for animal experimentation). These core facilities are available to researchers across the Unit, and externally, with care taken to maintain competitive pricing.

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

There are no major weaknesses, but it is surprising that some researchers have not yet attracted European PI-focused funding (e.g. ERC), which may represent missed application opportunities. In terms of minor points,

editorial responsibilities are present but are heavily dominated by Frontiers journals such that the portfolio could be more diverse. Additionally, of 32 presentations at international conferences, only five were by PhD students.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

Quantitatively, the IFM has published >140 research articles over the evaluation period, which is excellent. Qualitatively, the research is published in excellent to outstanding journals either generalist (e.g. Science, J Clin Invest, Cell Rep, Nature Comm) or among the best known in their fields (e.g. Brain, MolPsy, Development), and is internationally recognised as shown by high citation rates. In summary, scientific production is excellent to outstanding over the evaluation period.

- 1/ *The scientific production of the unit meets quality criteria.*
- 2/ *The unit's scientific production is proportionate to its research potential and properly shared out between its personnel.*
- 3/ *The scientific production of the unit complies with the principles of research integrity, ethics and open science. It complies with the directives applicable in this field.*

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

Standard 1: The institute has an unquestionable international visibility and reputation. During the evaluated contract, IFM has published 145 scientific articles. Sixty-three percent of the publications originate from the institute, and target journals are excellent and reputed in their field (for instance Brain, Development, Cell Rep, Hum Mol Genet, Mol Psychiatry, Nat Commun, Transl Psychiatry, J. Clin Invest, J. Physiol, Science...). Internal and external networking is highly efficient, as evidenced by the significant number of publications involving either at least two teams and/or a core facility of IFM on one hand, and with national/international collaborators. The visibility and expertise of IFM are also illustrated by several invitations to write reviews in highly reputed journals such as Science and Frontiers journals. During this contract, several publications were based on solid grounds and research projects were conducted with up-to-date technologies, so that several findings are innovative and promising for human health. All these elements, together with the established implantation of IFM within networks of excellence and success to grant applications, allow attraction of talented (and sometimes international) researchers and students.

Standard 2: Scientific production (publications, patents, databases) is excellent, and in general proportionate to the size (varying from 2 to 14 people) and maturity of the teams. Most members of the institute contribute to publications, whatever their status. Research projects benefit from internal collaborations and from many regular internal inputs (technical, conceptual), in a constructive way. Researchers aim at favouring quality over quantity, being selective in the target journals and making all efforts to obtain high-quality results. Junior groups are at a key moment in their evolution, and must capitalise on their seeding works. All three junior PIs already have a promising trajectory, as exemplified by the oldest junior group, which already has an excellent level of publication, a patent and links with industrial partners. Of note also, this junior PI has set up a core facility which benefits to several members of the institute. PhD and post-docs, despite the pressure of time, publish well. Senior groups also have excellent records of production (with nearly 5 productions yearly), both for their own projects but also for the collaborations they develop. Members of these senior teams publish original articles and are recognised experts, as shown by the important number of reviews (37) co-authored in prestigious journals.

Standard 3: IFM is exemplary regarding scientific integrity, ethics and open science. IFM follows all principles required by institutions and intellectual societies. The use of lab books ensures the traceability and reproducibility of the results. There is a strong culture of training and sensibilization to good practices/scientific integrity for new incomers, and a very interesting permanent willing to consider negative results as important results, and to discuss/criticise collectively raw data and technical issues. The unique initiative of JA Girault, published in eNeuro, is also an asset to ensure quality research. All ethical requirements for the use of humans/human cells/human tissues for research are or are about to be obtained (Codecoh declaration, consent forms...). Similarly, all ethical requirements for the use of rodents are respected (animal well-being internal committee,

use of Apafis for the evaluation of projects, regular training and informative update on evolution of ethical issues, licenses for surgery/project conception...). The IFM adheres to Open Science initiatives, including making results/datasets/software/methodologies openly available and publishing preprints (bioRxiv). For example, manuscripts are either published as Open Access, or deposited in the HAL repository.

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

Thirteen of 32 researchers do not yet hold the HDR. This may be a way to equilibrate the number of PhD students in each team (currently ranging from 1 to 12) and to share coordination, at the benefit of scientific production.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The unit has an excellent record in integrating basic research in a translational framework. They filed five patents with limited interactions with pharmaceutical companies, but displaying numerous clinical interactions. Pls strongly contributed to multiple foundations' scientific committees. The unit is also clearly engaged in disseminating its accumulated knowledge under different forms (national days on brain research or on research) and to various publics of different ages. Their participation in the regional networking C-BRAINS, bringing together academic laboratories and numerous companies, is a clear opportunity to reinforce socio-economic links and to communicate the progress of their research to the lay public.

- 1/ The unit stands out for the quality and the amount of its interactions with the non-academic world.*
- 2/ The unit develops products for the cultural, economic and social world.*
- 3/ The unit shares its knowledge with the general public and takes part in debates in society.*

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

Standard 1: nonacademic interactions

The unit interacts with industry in several ways: collaborations with biotech companies (AtmoSR, STEMCELL Technologies), consulting activities and scientific advisory board of pharmaceutical companies. Importantly, the unit takes part of the regional-networking C-BRAINS, which includes 40 companies offering the opportunity to establish novel collaborations with industrial partners.

Several team members (4) display a strong commitment to charities and foundations. They participate to scientific panels, contribute to their research strategy and perform grant reviewing (*Federation pour la Recherche sur le Cerveau* FRC, French Foundation for Research Epilepsy, Fyssen Foundation, ...). They also organise actions to share knowledge with patient associations (days for families), discuss ethical issues in stem cell research in national and international conferences, etc. Their research highlights are regularly relayed by the press service of the supervisory bodies, scientific journals in French or on YouTube, given the societal impact of their discoveries affecting neurodevelopment.

Regarding cultural interactions, the unit welcomes a doctoral student and artist from the SACRe graduate program of PSL University and a team leader is a member of the scientific council of the 'Fondation des Treilles' mixing science, literature and art.

Standard 2: Interactions with the socio-economic world:

The unit forged numerous links with the socio-economic world, although team activities concern primarily basic research. To foster these links, they organised incentive actions such as a yearly visit of the valorisation agency (Inserm-transfert) with a presentation of team's project.

Over the contract period, they filed five patents most often with international extension, and one US patent with a team leader as a co-inventor; one patent has been licensed to develop a commercial kit.

They display numerous interactions with clinicians mainly related to neurological and psychiatric disorders. They gave seminars to clinical audiences (European epilepsy network; Congress of joint European Neonatal Societies; ...). Teams participate in several networks gathering biologists and clinicians giving them excellent opportunity to set up collaborations and offering grants to support projects (*PEPR ProPsy*, *IHU Institut du Cerveau de l'Enfant* (children's brain institute with a specific interest for ASD)). Of note, the unit also hosts a translational program on neurodevelopmental disorders dedicated to reinforce connections with medical research. In collaboration with clinical geneticists, members of this program identified the molecular mechanisms underlying early postnatal fulminant neurodegeneration (*J. Clin Invest*, 2019) and collaborated with neuropathologists to translate that finding into clinics (two grants including 'Carnot Maturation Grant' obtained to test their molecule as adjuvant for brain tumor treatment).

Among other activities related to the socio-economic world, they participate in the writing of a national protocol for diagnostics and care for medical doctors and, were involved in the creation of an interface 'ValDEV', for the families of children suffering from 'Valproate' Syndrome.

Standard 3: Sharing of knowledge with the general public

The unit contribute to education of young people. They welcomed high school students and participated in programs such as *Apprentis-Chercheurs*, *Déclics*, *Cerveau en Seine*. A PI spent one to two half-days/year in public high schools to present the work of the team, another one participates in the 'forum des métiers en college'.

Their outreach activities are multiple and they encourage researchers to take advantage of the training offered by supervisory bodies for easy communication with lay public. They generated a promotional video of their activities, communicate with numerous media including national newspaper (*Le Monde*, *Le Parisien*, *La Provence*) and participate to radio or TV shows (*Le Magazine de la Santé*, *France 5*). They strongly contribute to yearly events (*Brain awareness week*, *fête de la science*, ...) and a member of the unit is very active in a society aimed to introduce neuroscience research to the general public (*Cerveau en Seine*) and was part of the organising committee of the 'Neuroscience' exhibition at SU in 2019. These actions will be pursued in the future since one goal of the C-BRAINS initiative is to communicate on the progress and challenges of research in neuroscience and cognitive science to the lay public.

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

Collaborations with companies could still be improved (for example, there are currently no students with academic-industry funding such as *CIFRE*). The C-BRAINS network should offer novel opportunities.

The departure of several members of the unit could hinder their contribution to the socio-economic world.

ANALYSIS OF THE UNIT'S TRAJECTORY

Not Applicable. The unit will close and most teams are joining the future *NEURO-SU* unit in the Pierre and Marie Curie campus, and others are joining the *ICM*, the *ESPCI* or the *IJM* units in Paris.

RECOMMENDATIONS TO THE UNIT

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

It will be critically important to pay attention to the impact of the staggered departure of teams during the transition period. At one point, there may be only four teams left at IFM, awaiting the move to NEURO-SU. All efforts should be made to ensure that integration into NEURO-SU begins before the move, particularly given that the date may change.

In the same vein, it will be important to plan management of the core facilities to maintain their functioning up until the moving date.

The institute demonstrates commitment to diversity, nevertheless, continuous efforts are required to monitor and address any emerging challenges or biases in the recruitment and retention processes. Similarly, the effectiveness of gender equality initiatives, such as participation in gender committees, needs ongoing evaluation to ensure meaningful impact and continuous improvement. Regular assessments of gender ratios across personnel categories are crucial to identify and rectify any potential imbalances in the long term.

Pending reports from the on-site visit by Ministry inspectors may highlight areas for improvement, and the institute should be prepared to address any suggested recommendations promptly.

Recommendations regarding the Evaluation Area 2: Attractiveness

The Unit is currently highly attractive. We recommend that strong efforts are made to integrate current practice into the future main hosting unit (NEURO-SU) in order to avoid dilution of this reputation and maintain strong international (but shared) identity.

Recommendations regarding Evaluation Area 3: Scientific Production

It is important that publications are not dominated by team leaders, and so we recommend reflection on publication strategies during review.

Small teams should be encouraged to publish consistently rather than wait for final production, in order to protect the career trajectory of researchers at all levels

Potential risks of a lower scientific publication levels relating to the upcoming move concern all teams. In their new units, they will need time to adapt and to get back to their normal rate of work. This can particularly endanger junior teams that need to promptly publish.

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

The unit is making strong efforts to develop relationships with industry, which are currently present but limited. We recommend making use of potential opportunities within C-BRAINS to build these links.

TEAM-BY-TEAM OR THEME ASSESSMENT

Team 1: Neurotransmission and signalling
 Name of the supervisor: Jean-Antoine Girault

THEMES OF THE TEAM

The team is deciphering the signalling pathways activated by Dopamine in striatal neurons and their alterations in neurological and psychiatric diseases. Using state of the art high-throughput strategies, they identified the differences in epigenetic DNA modifications and translating mRNA between the two main populations of striatal neurons. This led to the original observation that prostaglandin E2 plays a role of neuromodulator in the dorsal striatum. They develop powerful mouse models to get insights into a mutation in a gene involved in signal transduction in striatal neurons responsible for dystonia in humans. They previously identified a non-receptor tyrosine kinase (Pyk2) highly expressed in the hippocampus and characterised its role in synapses and its involvement in diseases.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

In the previous report, there were no major recommendations regarding scientific production and activities or on the team's organisation and life. The committee encouraged the team to maintain their high level of scientific outputs and activities. As detailed in the following section 'strengths', this has largely been successful regarding all aspects of this criteria (e.g. €2.7m funding secured over five years; publication in highly reputed journals such as Science, eLife, Nat Comms). This team has thus maintained its national and international commitment and reputation.

The previous committee had advised the team to identify key projects to focus on, so as to stand as leaders with regard to the international competition. The team has thus made strategic choices to focus upon three projects: (1) transcriptional and epigenetic mechanisms underlying differences between striatal neuronal populations (2) the role of mutations in signalling proteins in movement disorders (3) the role of the non-receptor tyrosine kinase Pyk2 in physiological and pathological conditions. This has been a productive approach, as indicated by publications in high-profile journals (e.g. eLife, Nature Communications).

Overall, the recommendations helped the team to maintain its unquestionable quality and reputation up to its term.

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

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

EVALUATION

Overall assessment of the team

The team's scientific output is outstanding (41 publications, 21 as lead including in top journals such as Mol Psy., Nature Com.). They welcomed three PhD students and six post-docs, all from abroad (Europe, Japan) and had several international collaborations (Italy, Japan, UK, USA). Numerous indicators show their very high reputation at national (one PI is among the top-cited scientists in Neuroscience) and international levels (PIs act as President of the FENS and onERC panel). The funds raised are outstanding (~3M€) including at the European level (Eranet Neuron). The team contributes to social-economic world (1 EU and US patent,) and participates in several outreach activities. The committee considers that the team is outstanding overall.

Strengths and possibilities linked to the context

The team, via its two senior researchers, has obtained an outstanding level of funding (total budget of 2.7M€ over five years, mean 363 k€/year), and the budget is secured until the end of 2024. Resources arise from institutions, international contracts, national (1.181M€ over 5 years, mean 197 k€/year) or European/international (797 k€ over 5 years; mean of 133 k€/year) competitive calls including 1 COPOC, 4 ANR (including 3 as leader), one EraNet Cofund JPND (as partner), as well as foundations (FRM, FDF, FMR).

An important part of the quality/visibility of the team relies on its team leader, who is an emblematic figure within Neurosciences, both nationally and internationally. Among his impressive record of achievements (many of which benefit of the community), one can mention a series of responsibilities ((vice presidency of the Société des Neurosciences and the FENS) and their attendant events (FENS meeting, Neurofrance...), participation in scientific/institutional boards (INSERM, University, various foundations/charities...), and invitations to give conferences/inaugural lectures. Of course, these achievements ensue a scientific career of major discoveries, including those (past and ongoing) from the team. Altogether, members of the team have an outstanding scientific contribution (41 publications of which 6 reviews, 33 original articles, 2 book chapters, and one patent; equilibrium between the number of publications led by the team versus resulting from a rich network of collaborations). This largely contributes to the attractiveness of the team for young students (3 PhD and 7 Post-docs, several coming from abroad). The work of the team uses up-to-date technologies and is published in highly reputed journals such as Mol Psy, Nat Commun, eLife, J. Neurosci, Science, CDD, highlighting the expertise of the team in the pathophysiology of dopaminergic neurons in the striatum.

The contribution of the team to teaching is also significant, and it has trained various kinds of students ('têtes chercheuses', masters and PhD). PhD (3 out of 4 have graduated in the period) and post-docs have published at least one article as first author. Professional insertion of former lab members is strong; all three PhD graduates have secured research positions, two of which are international (Israel; Japan). Finally, the interaction of team members with society is also important, on several occasions such as la fête de la science or conferences for a lay audience.

Overall, the team will close with an outstanding track record.

Weaknesses and risks linked to the context

There are three researchers/faculty but their visibility/productivity is unbalanced, and not all of them published as senior authors: the mean number of signed articles ranges from 0.2 to 6.1 publications per year.

Analysis of the team's trajectory

One PI retired in September 2023 and the team will cease its activities in December 2024 (budget secure until the end of 2024). The other people with permanent positions will join other teams. Importantly, it is mentioned that 'part of the scientific activity will be pursued by former team trainees located in different institutes' which is encouraging in view of the remarkable scientific advances made by the team.

RECOMMENDATIONS TO THE TEAM

Since the team will close, there is no recommendation to formulate, apart from making sure that the last staff members with permanent position benefit from an optimal integration in their future hosting group.

Team 2: Cortical development and pathology
 Name of the supervisor: Fiona Francis/Laurence Goutebroze

THEMES OF THE TEAM

The team's focus revolves around investigating the mechanisms involved in cortical development, with the primary goal of uncovering novel regulatory and dysregulatory processes affecting cortical cell types during corticogenesis. During the evaluated period, they revealed key disrupted pathways contributing to the formation of abnormal brain circuits. For instance, they identified new gene mutations in patients with cortical malformations and revealed unexpected molecular and cellular patho-mechanisms for heterotopia.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The first recommendation of the previous committee was not valid as there was obviously a mistake in the report pointing to a lack of integration of a translational activity, clinical collaborations and industrial contracts. The team leaders provided factual elements to argue against this and demonstrated that it was not the case.

Second, it was advised to be careful about the risk for the team leader to be overwhelmed by an important additional load of work due to her new responsibilities in the directorship of the institute, thus affecting the current team organisation and life. Accordingly, in the evaluated period, all team members participated actively in the supervision of students and post-docs, were attentive to the well-being of everyone in the team, and were importantly involved in the advancement of all projects, thus all contributing to the success of the entire group. Finally, the team leaders made efforts to better integrate their two major interests by applying conjointly at two grant applications and by continuing developing interactions with clinicians to advance translational aspects of their research.

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	6
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	2
Doctorants	3
Sous-total personnels non permanents en activité	5
Total personnels	11

EVALUATION

Overall assessment of the team

Team 2 is an outstanding team, composed of five PIs, two postdoc, three PhD and one permanent technical staff. The scientific production is excellent to outstanding (26 peer-reviewed articles, 15 signed as last and 14 as first author, 13 with doctoral students) in renowned journals (e.g. Science, Nat Comms). The funding level is outstanding (2 ANR, 2 ERANet, 2 FRC and 1 FRM, total > 2 M€). Student training is excellent with 6 PhDs supervised and three defences during the period (3 more to come in 2023). Outstanding visibility is attested by organisation and invitations in national and international meetings and in scientific panels (ERC, FENS programs, etc.).

Strengths and possibilities linked to the context

The scientific production of the team is outstanding. The team topic addresses mechanisms underlying cortical development and aims to discover new regulation/dysregulation processes of cortical cell types during corticogenesis. Their work resulted in the publication of 26 articles, some in highly ranked journals (Science (1), Nature Communication (1), J Cell Biol (1), Current Opinion in Neurobiology (1), EMBO Reports (2)). These publications were signed as first and/or last authors for the majority (14 first, 15 last), and were co-authored by students and technical staff of team, which illustrates the recognition of the work and implication of every team member. Every PhD student and post-doctoral fellows had at least one paper as the first author.

The team has shown an outstanding ability to raise funds with several national and international competitive grants, such as two ERA-NET, two ANR, two FRC, one FRM for a total budget above 2M€, being PI or coordinator for all of these grants except one ANR. Projects are secured up to 2025.

The team is internationally recognised in the field investigating the mechanisms underlying early development of the cortex in normal and pathological contexts. They built a large network of robust and productive collaborations in the field of neurodevelopment and pathology. This results in the team leader being importantly involved in coordinating several ERA.NET projects, participating in ERC grant panels and other multiple national and international grants, organising meetings (FENS, Club DRN, IFM colloquia), being part of numerous steering committees and team members being awarded by recognised prizes (from FRM, ARC, Fondation de France, Epilepsy Foundation, ...).

The team is also significantly involved in teaching and training with six PhD students (4 from foreign countries such as USA, Spain and Italy) having been trained during the evaluated period, 27 in total at all levels from undergraduate to graduate and two associate professors teaching at Sorbonne University and with responsibilities in course organisation and design. This activity definitively contributes to the attractiveness for students.

Regarding the contribution to society, the team performs extremely well as it has been involved in the creation of an interface for the family and children suffering from the Valproate Syndrome. The two team leaders also took part in a working group for the writing of a national protocol for diagnostic and care for physicians in this pathological context. They also gave seminars on several occasions to large clinical audiences and interacted on a regular basis with patient associations and public audiences.

Weaknesses and risks linked to the context

No major weakness could be identified by the committee.

Analysis of the team's trajectory

Not relevant here as the team moves to the Neuro-SU unit.

RECOMMENDATIONS TO THE TEAM

The team moves to the Neuro-SU unit around 2025. However, the move to Neuro SU might slow down a bit the productivity during the first period of the next contract, a risk that could be compensated for by the high quality of the research performed in the team. The team has a great potential to publish more often in prestigious journals in leading positions.

Team 3: Plasticity in cortical networks and epilepsy

Name of the supervisor: Jean Christophe Poncer/Sabine Lévi

Since this team is moving to ICM and ESPCI, its evaluation was considered at ICM and ESPCI.

Team 4: Migration of cortical interneurons
 Name of the supervisor: Christine Métin

THEMES OF THE TEAM

The aim of the team was to decipher the role of physical or chemical extrinsic signals in controlling the migration of GABAergic cortical interneurons (cIN) from the basal forebrain to the developing cortex. Migration defects may lead to inhibitory circuit abnormalities in the cortex and related neuropsychiatric disorders. Over the period the team mainly focused on the role of cell adhesion and signalling mechanisms acting at the primary cilium in cIN migration. To reach their goal they developed various in vitro, ex vivo and mouse models.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team was asked to continue publishing in highly regarded journals, to integrate the two new senior researchers and to pursue translational research. The team continue to publish in highly regarded journals (Biomaterials, Brain, PNAS). The two senior researchers who joined the team integrated very well as illustrated by their contribution to the team project (one article came out for one, another is in preparation for the second one). The translational aspect of the research was pursued as illustrated in a Brain publication (2020). An additional comment was to focus the research project, which was indeed the case with a main focus on the primary cilium in interneuron migrations in the cortex.

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

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

EVALUATION

Overall assessment of the team

The team's scientific output is excellent to outstanding (24 publications, 7 as lead including PNAS, Brain). Several items illustrate their attractiveness and visibility at the national and international levels. They hosted two new researchers, two PhD and two post-doc, established fruitful collaborations (11 papers in eLife, Nature metabolism, etc.) and were invited to perform evaluations (ERC, ANR grants). Team members belong to INSERM and CNU national councils and one PI is deputy director of a department at the university. Their ability to secure money is excellent. Team members are also involved in outreach activities. The committee considers that the team is excellent to outstanding. They made several major contributions to our understanding of the mechanisms controlling cINs migration. They showed that specific cadherin-related proteins are essential for cIN to reach definite functional cortex areas (PNAS, 2017). They developed new technologies at the interface of biology and biophysics (coll. Institut Curie) and deciphered the role of topographical cues in cIN migration (Biomaterials, 2019). Another important contribution to the field concerns the signalling mechanisms activated at the primary cilium regulating cIN migration. They developed a genetic tool to manipulate subcellular signalling (Cell Rep. 2020) and identified the role cAMP/cGMP ratio in the regulation of cell polarity (BioRxiv, 2023). They also identified a mutation in the autosomal Y1F1B gene causing Golgi and primary cilia abnormalities associated with neurodevelopmental delay in human (Brain 2020).

Strengths and possibilities linked to the context

Over the period, the team was composed of five permanent researchers (3 researchers, 2 faculty), two engineers, two PhD and two post-docs.

The team's scientific output is excellent to outstanding with 24 publications, including eighteen original articles, seven signed by team members as first or last author in top journals (PNAS, 2017; Biomaterials, 2019; Brain 2020), 4 invited reviews and two book chapters. Members of the team are also collaborators on eleven publications including in high-ranked journals (eLife, 2019; Nature Metabolism, 2021).

Over the period, the team trained two PhD students (1 PhD, first author in Biomaterials and a book chapter) and attracted two post-docs (Co-author in Cell rep. 2020; 2 papers in revision; 1 review as first author).

Two team members are remarkably active in teaching. One faculty member co-leads the Neuroscience division; the other is the deputy director of an innovative pedagogy department and coordinates Scientific communication and Mediation Units.

The attractiveness and visibility of the team is excellent. The team attracted two colleagues at the start of the period, welcomed two PhD students and two post-doc (one from abroad). They set up several collaborations, three national and one international (Canada). PI organised and chaired a symposium at the French Neuroscience Society meeting (2017), they were invited to thirteen oral presentations including national and international conferences and seminars. A team member was selected for oral presentation to two international meetings. They contributed to the evaluation of national and international grants (ERC, ANR) and are members of national scientific committees (CSS4 Inserm, CNU).

The team's ability to secure funding is excellent (>850k€ mainly as coordinator) from national (ANR as partner Labex as coordinator) and international (one single competitive young investigation award from BBRF) research grants and foundations (FMR, FRM, as coordinator).

Team members are involved in outreach activities through regular interventions in schools (Déclics program), participation to the 'Forum des métiers en collège' and U-Tube communication.

Weaknesses and risks linked to the context

No publications even in preparation are listed for one post-doc (2016–2019) and the last PhD student. This may represent a risk for them, particularly in the context of the retirement of the PI and the closure of the team. Of note, no patents were submitted.

Analysis of the team's trajectory

The team is closing following the retirement of the team leader (April 2023). Some team members will join team 5 until finalisation of their publications. The trajectory seems already set up for the team members thereafter.

RECOMMENDATIONS TO THE TEAM

The main recommendations are to be particularly attentive to ensuring that publications in progress are finalised and to make sure that the staff members with permanent position benefit from optimal support to integrate future hosting groups or research units.

Team 5: Serotonin, Microglia, Plasticity and Disease
 Name of the supervisor: Luc Maroteaux/Anne Roumier/Corentin Le Magueresse

THEMES OF THE TEAM

The main direction of the team is to study neuroimmune interactions in normal and atypical brain development, and the involvement of these interactions in neurodevelopmental psychiatric disorders.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has actively implemented the recommendations from the previous report. Firstly, in response to the criterion 1, suggesting to maintain scientific excellence, level of publications and funding from multiple sources, the team has maintained an excellent level of scientific output and publications (34 original articles, 8 as leader, and one patent). They secured funding from various sources, including ANR, FRC, ERANET, Fondation de France, and the Emergence program of Sorbonne University.

Secondly, aligning with the suggestion to develop new therapeutic strategies related to 5-HT2B receptors, the team initiated a collaborative project on microglial HTR2B function in memory. Additionally, they leveraged expertise in electrophysiology, characterising conditional HTR2B KO in the brain, with relevant research findings in press (Mol Psychiatry).

Regarding the third recommendation on team organisation (teaching duties of the co-leader particularly), the team proactively addressed the increasing involvement of the co-team leader who received a teaching load reduction and plans to apply for IUF and to participate in Sorbonne University's APACHES program.

Concerning the recommendation for permanent researchers to defend HDRs for PhD recruitment and career advancement, both PIs defended their HDRs since the last HCÉRES evaluation.

In response to the recommendations to pursue their excellent scientific strategy and projects, the team sustained their excellent scientific activities by consistently applying to diverse funding sources and initiating/strengthening collaborations in France and abroad.

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	0
Sous-total personnels permanents en activité	4
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	3
Total personnels	7

EVALUATION

Overall assessment of the team

This medium-size team (4 PIs) brings extensive expertise to the field of neuroimmunology with three major achievements: they showed the requirement of serotonin receptor 5HT2BR in microglia during the development to limit neuroinflammation in adulthood, the beneficial role of these receptors in depression, and the elevated expression of complement C4 in prefrontal cortex of schizophrenia models. They have a collaborative network spanning France and Europe and secured funding from various sources (Eranet Neuron as partner, two ANR as leader FRM, FRC, FDF and six Labex grants mainly as coordinator). Notably, the team published 34 original articles, with contributions in excellent journals like Circulations or Nature neuroscience. However, their contribution as leading authors is in very good to excellent with eight publications with team members as first or last authors, along with seven reviews, one book, and four book chapters. Four doctoral students successfully defended their theses, with two more scheduled for 2023. Overall, this is a very strong and dynamic team, recognised for its work as shown by their contribution to organise highly visible symposia (FENS Hertie School Keystone symposia...).

Strengths and possibilities linked to the context

The team has demonstrated an outstanding ability to raise funds, securing 1.6M€ over the past mandate, and has successfully attracted postdocs and new established scientists. One PI is a co-inventor of a patent focused on the use of a serotonergic receptor antagonist for treating and preventing heart damage in mammals. The team actively participates in general public communication and educational initiatives.

Furthermore, the team possesses unique expertise in flow cytometry within the institute, overseeing two flow cytometers. Additionally, they manage two patch-clamp rigs equipped for multi-cell recordings and optogenetics. With these resources, the team is well equipped with the necessary expertise and skills to advance their research. PI organised symposia s (FENS Hertie School, symposia at the Meeting on Clial cells and Health and disease and a keystone symposia).

Weaknesses and risks linked to the context

No weaknesses were identified by the committee, except that no European or international funding was obtained during the mandate as coordinator.

Analysis of the team's trajectory

In the next mandate, the team will join the Institut de Biologie Paris Seine.

RECOMMENDATIONS TO THE TEAM

We suggest that the team should pursue its excellent work by maintaining its excellent visibility in the field (prize, organisation of symposia) and by applying to European grants.

Team 6: Sleep and Emotional Memory
 The name of the supervisor Gabrielle Girardeau

THEMES OF THE TEAM

The team studies the role of the different sleep stages in the consolidation of memories involving an emotional component, the influence of emotions or emotion-related factors such as stress and anxiety on memory, and the regulation of emotional reactivity. Their approach is based on a large-scale, multi-structure electrophysiological recordings in freely behaving (learning/sleeping) rodents that allows recording of a growing number of independent neurons as well as local field potentials. To investigate causality, they implement closed-loop paradigms in which neural patterns are detected and perturbed in real time with optogenetics.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Not relevant as this is a new team recruited during the last term.

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	0
Sous-total personnels permanents en activité	2
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	1
Doctorants	3
Sous-total personnels non permanents en activité	4
Total personnels	6

EVALUATION

Overall assessment of the team

This small team (2 PIs) was created through an ATIP-AVENIR contract for 2019–2023, and has shown previous excellent production. Despite its youth, the team leads an impressive and promising research program and has shown outstanding attractiveness: it has already attracted a novel permanent researcher (MCU) and self-funded PhD students and post-doc. Importantly, the projects are mostly already financed until 2026 (>700k€ including 2 ANR grants - 1 as coordinator). The projects are highly original and innovative but still need to lead to publications to secure the team. Overall, the research done is excellent and promising.

Strengths and possibilities linked to the context

The team has shown an outstanding ability to raise funds and attract permanent researchers and students. It is notable that despite a creation *ex nihilo* in 2019, the team has already 6 persons with one researcher, one teacher researcher, three PhD students, two Post-docs, and one short-term contracted engineer. Projects presented are of outstanding quality and based on state of the art approaches with a focus on networks of episodic memory and emotions (hippocampus, amygdala, and later prefrontal cortex (PFC)). The methodological approach is very original with innovative protocols based on closed- and open-loop large-scale and multi-structure in-vivo electrophysiology (MUA, LFP) and optogenetics, during spatial learning,

emotional learning and emotional experiences, and during sleep. The team has all the skills and technical environment to design and carry out the protocols with the relevant hired multidisciplinary expertise (biological, psychological, computational).

The team obtained a young investigation award from the competitive BBRF foundation and one grant emergence from the city of Paris as well as support from foundation (FRM, FSER, Fyssen) for a total amount > 400K€ in addition to their ATIP avenir support (340 K€ for the 2019–2023 period).

All members of the team were involved in communications with the public, through Declics (interventions by all actors of science in high schools), various organisations for the dissemination of science (F93, Palais de la découverte, semaine du cerveau), and welcoming high school students in the lab for short 'discovery' internships.

Weaknesses and risks linked to the context

There are two possible weaknesses that are intrinsic to this team. First, major publications are still to be delivered. This is expected as the team is very young and uses complicated in vivo approaches. Second, the move to the NPS unit will have to be secured, in particular for the sophisticated experimental set-ups that will have to be moved with care to the Cassan building in the NEURO-SU environment.

Analysis of the team's trajectory

The team moves to the Neuro-SU unit and will be evaluated in its future hosting unit.

RECOMMENDATIONS TO THE TEAM

The committee recommends to the team leader to focus on publishing their exciting results, in order to maintain their financial leverage capacity and allow early career researchers to be competitive on the job market.

Team 7: Stem cells & Neurodevelopment

Name of the supervisor: Stéphane Nedelec

THEMES OF THE TEAM

Established in June 2016 at the Institut du Fer à Moulin, this previous ATIP/Avenir team focuses on unravelling the fundamental principles of human nervous system development in health and disease. Their research involves histological analysis of human embryos, 3D differentiation of human pluripotent stem cells, live imaging, transcriptomic analysis, and bioengineering. The team's objectives include deciphering pathways and physical constraints in hindbrain and spinal cord morphogenesis. They utilise these developmental principles to optimise differentiation into specific human cell types or organoids, contributing to the understanding of pediatric diseases.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Not applicable, the team started in 2016 and was not evaluated in 2017.

WORKFORCE OF THE TEAM: IN PHYSICAL PERSONS AT 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	2
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	3
Sous-total personnels non permanents en activité	3
Total personnels	5

EVALUATION

Overall assessment of the team

The team was established in June 2016, and despite its small size (1 PI) has made significant contributions, publishing four original articles in renowned journals (i.e. Nature Comms and Neuron) and depositing three patented protocols. Community recognition is also strong (e.g. 2 editorial highlights in Development). The team has demonstrated academic success with two doctoral students defending their PhD theses, who authored papers and are both authors on a patent. Overall, this is an excellent team.

Strengths and possibilities linked to the context

The team has gained significant recognition in the field of in vitro human embryogenesis, demonstrated by well-cited articles, collaborative reviews, and active participation in international networks and consortia and were invited to present in national or international conferences such as Cold Spring Harbor, Joint meeting of Dev. Biology societies meeting, Neurofrance. It had three PhD students in co-direction, and they are affiliated with Moddulo, an international network uniting teams from the US, Europe, and Japan. Furthermore, it contributes to

initiatives such as DIM C-BRAINS organoid and Sorbonne University's stem cell program. The team secured competitive funding, including two ANR grants as partner, one AFM grant as coordinator, ATIP/avenir, and Chaire d'excellence LABEX for a total funding of ~800K€ after their ATIP-Avenir funding. Funding was also obtained for equipping the tissue engineering facility. SN holds positions in key scientific bodies, including the scientific council of ARSLA and the scientific board of Sorbonne University's Stem Cell Initiative. The activity of the team was organised around the development and the use of new *in vitro* models derived from human pluripotent stem cells (hPSCs). Their investment in the technological advance in the field is demonstrated by the wide use of their differentiation strategies, and notably by the three patented protocols, one of which is licensed to develop a commercial kit. The team used these models to investigate signalling pathways controlling the differentiation and morphogenesis of the hindbrain and spinal cord, and published their work in field journals, and more recently in a more general and excellent journal. This work opens avenues for future research, indicating the potential of these models to lead to important findings and facilitate the combination of various techniques, including omic and imaging methods.

Weaknesses and risks linked to the context

The team needs to grow and to attract ambitious postdocs and/or permanent scientists with complementary expertise to fully develop the projects, and current fundings are ending in 2024. These risks are mitigated given that in the future mandate, the team will fuse with the team of Vanessa Ribes at *Institut Jacques Monod* (Paris) to gain in size and expertise.

Analysis of the team's trajectory

Not relevant here as the team moves to Institut Jacques Monod.

RECOMMENDATIONS TO THE TEAM

The future of this team will be evaluated at the Institut Jacques Monod.

Team 8: Pleiotropy of morphogens

Name of the supervisor: Julien Ferent

This team is an ATIP-Avenir that started in 2021 and will then not be evaluated.

CONDUCT OF THE INTERVIEWS

Date(s)

Interview conducted: on files

INTERVIEW SCHEDULE

Not Applicable.

PARTICULAR POINT TO BE MENTIONED

Not Applicable.

GENERAL OBSERVATIONS OF THE SUPERVISORS

Marie-Aude Vitrani
Vice-Présidente Vie institutionnelle et démarche
participative
Sorbonne Université

à

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

Paris, le 29 mai 2024

Objet : Rapport d'évaluation **DER-PUR250024401 - IFM - Institut du fer à moulin - 0755890V**

Cher Collègue,

Sorbonne Université vous remercie ainsi que tous les membres du comité HCERES pour le travail d'expertise réalisé sur l'unité de recherche « IFM ».

Sorbonne Université n'a aucune observation de portée générale à formuler sur le rapport d'évaluation transmis.

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

Marie-Aude Vitrani
Vice-Présidente Vie institutionnelle
et démarche participative



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