

EVALUATION REPORT OF THE UNIT
INMED - Institut de neurobiologie de la
Méditerranée

UNDER THE SUPERVISION OF THE
FOLLOWING ESTABLISHMENTS AND
ORGANISMS:
Aix-Marseille Université

EVALUATION CAMPAIGN 2022-2023
GROUP C



In the name of the expert committee¹ :

Mr. Philippe Marin

For the Hcéres² :

Mr Thierry Coulhon, President

Under the decree n° 2021-1536 of 29th November 2021:

¹ The evaluation reports "are signed by the chairperson of the expert committee". (Article 11, paragraph 2);

² The president of the Hcéres "countersigns the evaluation reports established by the expert committee and signed by their chairperson." (Article 8, paragraph 5).

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

MEMBERS OF THE EXPERT COMMITTEE

Chairperson: Mr Philippe Marin, CNRS, Montpellier

Mr BROCCOLI Vania, Institute of Neuroscience, Italy

Ms DEROCHE-GAMONET Véronique, Neurocentre Magendie, Bordeaux

Mr HANTRAYE Philippe, MIRCen, CEA

Ms ANGULO Maria Cecilia, Inserm

Experts: Ms DEHAY Colette, Institut cellule souche et cerveau, Lyon, (Representative of Inserm CSS4).

Mr TREMBLEAU Alain, Sorbonne Université, Paris, (Representative of CNU 69)

Mr BOURDONCLE Pierre, Plateforme Cochin, Paris (Representative of supporting personnel).

HCÉRES REPRESENTATIVE

Mrs Nadia Soussi-Yanicostas

CHARACTERISATION OF THE UNIT

- Name: Institut de neurobiologie de la Méditerranée
- Acronym: INMED
- Label and number: UMR1249
- Number of teams: 9
- Composition of the executive team: composition of the executive team

SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement

SVE5 Neurosciences et troubles du système nerveux

THEMES OF THE UNIT

The research project developed at INMED aims to understand at the neuronal circuit level the plasticity mechanisms that operate during brain development, learning and various neuro-pathologies, including epilepsy, autism spectrum disorders, Alzheimer's disease, Parkinson's disease, and schizophrenia. The goal is to bridge the gap between early developmental programs and information coding in adult brain circuits. This project relies on complementary experimental strategies, from molecules to behaviour, with a strong core of electrophysiological, imaging, and behavioural approaches combined with gene delivery using viral vectors or *in utero* electroporation in rats and the use of a large variety of pre-clinical models.

The INMED is organised in ten research teams (eight INSERM/AMU-labelled teams, one ERC Starting team and one Chair of Excellence) that independently develop their own project in frame of the general topics of INMED. All these teams combine expertise in neuronal physiology, molecular and cell biology as well as behaviour. They share resources, tools and expertise and benefit from a common core of scientific and technological platforms.

- Team 1 investigates the mechanisms controlling brain development and maturation that are involved in the pathophysiology of neurodevelopmental disorders, such as epilepsy, intellectual disability, or autism spectrum disorders.
- Team 2 investigates hippocampal function at circuit level in health and disease, and how it is constrained by early developmental genetic programs and activity-dependent processes.
- Team 3 investigates the pathophysiological mechanisms leading to seizure generation, impaired rhythmogenesis, and behavioural comorbidities in epilepsy and autoimmune diseases.
- Team 4 (ERC starting) investigates the network and cellular determinants allowing spatial navigation skills, their development and alteration in various diseases.
- Team 5 investigates the structural and functional development of the brain under physiological and pathophysiological conditions (brain hypoxia, trauma, autism spectrum disorders, intellectual disability, and epilepsy).
- Team 6 investigates how meso-corticolimbic microcircuits are shaped throughout early life critical periods such as adolescence, to give rise to harmonious emotional behaviours and cognitive functions in adulthood and how this is altered by environmental and genetic insults modelling neuropsychiatric diseases.
- Team 7 focuses on the role of two hormones (oxytocin, leptin) and of chloride homeostasis as critical neuromodulators of the maturation of neurons and neural wiring.
- Team 8 investigates the mechanisms underlying adaptive decision-making and motor control, with a focus on the dorsal striatum and its cortical inputs.
- Team 9 investigates the pathophysiological events associated with epilepsies and encephalopathies of genetic and non-genetic origins.
- The Chair of Excellence team investigates the inputs that pyramidal neurons of the visual cortex receive on their dendrites, the computations they can do, and the impact of their activity on eye movement.

The INMED also hosts one of the Centuri junior teams in theoretical neuroscience.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The INMED is a neuroscience research centre affiliated to INSERM and Aix-Marseille University located on the Luminy Campus. It is located in a unique building of around 4,800 m².

The INMED was founded in 1999, when most members of an INSERM unit located in the Port Royal maternity hospital (INSERM U29, ~30 people) decided to move from Paris to Marseille to implement a new research institute, dedicated to the pathophysiology of brain development. Its implementation on the Luminy Campus was in perfect harmony with the local scientific environment, especially with the presence of the Institut de Biologie du Développement de Marseille (IBDM) on the campus. The INMED shifted from an INSERM Unit to a Research Centre in 2012, concomitantly with the consolidation of its research groups into independent teams

and the creation of technological platforms. The last decade has been also marked the broadening of the INMED backbone expertise in electrophysiology towards analysis of genetic, molecular and anatomical properties of brain circuits and behaviour. The INMED has also broadened its research interests to various neurodevelopmental (autism, intellectual disabilities, Prader Willi) and psychiatric diseases (schizophrenia, addiction, etc.).

The last contract period has seen evolution towards a more quantitative, predictive and systems-level description of brain circuits that was partly supported by the use of calcium imaging approaches and the development of a local community of data scientists, theoretical neuroscientists and engineers in the frame of the creation of Centuri, an interdisciplinary centre located in Marseille, which explores the complexity and the dynamics of living systems and strongly collaborates with INMED teams.

RESEARCH ENVIRONMENT OF THE UNIT

The INMED has developed strong interactions with the local environment.

At the level of Luminy campus, the INMED shares with the IBDM (Institut de Biologie du Développement de Marseille) a new facility of 480 m². In addition, the INMED has ongoing collaborations with several teams from research units of the Luminy Campus, including the Center for Theoretical Physics, IBDM, LIS (Laboratoire d'Informatique & Systèmes) and CIPHE (Immunophenotyping centre). The INMED also recruited an INSERM research engineer by sharing the need with two neighbours, the UNIS (Unité de Neurobiologie des canaux Ioniques et de la Synapse) and the LAI (Adhesion and Inflammation Laboratory).

Over the past years, the INMED has significantly strengthened its participation and visibility in the University teaching programs, with eight associate professors/professors, including the head of the Master, Licence and PhD Biology programs. One INMED scientist is vice-dean of the university.

The INMED had a leading role in the implementation of several local structuring organisations. It has led the creation of NeuroMarseille institute, which gathers nine research institutes (3,000 people, <https://neuro-marseille.org/en/>) and the graduate school in neuroscience NeuroSchool (EUR). The goal of NeuroMarseille creation was to increase the attractiveness of the university, international collaborations, interdisciplinarity, links with the clinics and industry, and the integration of students into professional life. Many INMED scientists and engineers participate in NeuroMarseille committees (4 in two different NeuroMarseille committees). Four INMED teams received grants in 2020 and 2021 from this institute, and one PhD student was funded during the reporting period. It is a core member as the main experimental neuroscience institute of the Turing Center for Living Systems (Centuri, <https://centuri-livingsystems.org/>), a federative project that aims at deciphering the complexity and dynamics of biological systems. The INMED hosts one of the Centuri junior teams in theoretical neuroscience and has recruited seven PhD students and six postdocs thanks to Centuri calls. The Unit director is a member of the Centuri steering committee and the head of the Engineering committee. She has been organising the Centuri summer school every year since 2019. Its aim is to deploy innovative imaging technologies to monitor the emergence and plasticity of functional circuits during development and their dynamics during behaviour in health and disease throughout life, by tailoring commercially available instruments or transferring innovative technologies from optic labs to routine life imaging thanks to strong partnerships with industrial partners. It is a member of the Marseille Imaging (<https://www.univ-amu.fr/en/marseille-imaging>) and Rare Diseases (<https://www.univ-amu.fr/en/marmara>) Institutes. It has developed longstanding collaborations with the neurology, neurosurgery and paediatrics departments of Marseille University hospitals and is a founding member of the FHU Epinext and DHUNE, the latter being part of the 'Centres of Excellence on Neurodegenerative Diseases (CoEN)' network.

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

Permanent personnel in active employment	
Professors and associate professors	5
Lecturer and associate lecturer	4
Senior scientist (Directeur de recherche, DR) and associate	12
Scientist (Chargé de recherche, CR) and associate	19
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	31
Subtotal permanent personnel in active employment	71
Non-permanent teacher researchers, researchers and associates	4
Non-permanent research supporting personnel (PAR)	12
Post-docs	11
PhD Students	38
Subtotal non-permanent personnel	65
Total	136

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

Employer	EC	C	PAR
Inserm	0	20	26
CNRS	0	11	0
Aix-Marseille Université	7	0	3
APHP	1	0	1
CHU Marseille	1	0	1
Total	9	31	31

UNIT BUDGET

Recurrent budget excluding wage bill allocated by parent institutions (total over 6 years)	4,172
Own resources obtained from regional calls for projects (total over 6 years of sums obtained from AAP idex, i-site, CPER, territorial authorities, etc.)	240
Own resources obtained from national calls for projects (total over 6 years of sums obtained on AAP ONR, PIA, ANR, FRM, INCa, etc.)	8782
Own resources obtained from international calls for projects (total over 6 years of sums obtained)	9,066
Own resources issued from the valorisation, transfer and industrial collaboration (total over 6 years of sums obtained through contracts, patents, service activities, services, etc.).	175
Total in euros (k €)	22,435

GLOBAL ASSESSMENT

Over the past five years, the INMED has successfully developed a well-focused and timely line of research aimed at understanding at neuronal circuit level the plasticity mechanisms that operate during brain development, learning and pathogenesis. The originality of the INMED project relies on its capacity to bridge the gap between neurodevelopment and circuit physiology and dysfunction in the adult brain and provides the unit a unique positioning in France and abroad.

The INMED also stands out by its remarkable scientific production, with around 300 articles or reviews during the reporting period, some of them being published in wide readership generalist journals (Science, Nature Communications, PNAS, Elife, Cell Report, etc.) or top/high-ranked journals in the field of Neuroscience (Nature Neuroscience, Neuron, Brain, Molecular Psychiatry, Cerebral Cortex, etc.). Notably, more than one third of the INMED publications involve several teams of the unit and each team has a minimum of four publications shared with other INMED teams, highlighting the remarkable capacity of the INMED teams to generate synergies and their strong commitment in the scientific policy of the unit.

Collectively, the originality and the quality of the research conducted at INMED makes it one of the most visible, respected and attractive institutes in the Neuroscience field worldwide. Capitalising on this strong international recognition, the INMED has shown an outstanding capacity to raise funding, including funding dedicated to shared state-of-the-art equipment, in response to competitive calls from French, European and foreign institutions, and an outstanding capacity to attract talented young scientists who bring the unit their complementary expertise.

Over the reporting period, the INMED has also remarkably strengthened its interactions with the local scientific community, especially in the frame of the Aix-Marseille University IDEX Amidex. The unit has led the creation of the NeuroMarseille institute that gathers the local neuroscience community, the graduate school in neuroscience NeuroSchool and the Circuitphotonics Center. It is a core member of the Turing Center for Living Systems (Centuri), a federative project aimed at deciphering the complexity and dynamics of biological systems and has strongly increased its participation in the university teaching programs. The INMED is now perfectly integrated within the local community where it has a clear leadership, and it now fully benefits from all the opportunities provided by the IDEX and other local initiatives. Though the INMED has also established longstanding interactions with Marseille University Hospital, the collaboration between the unit and clinicians can certainly be reinforced given the translational potential of the research carried out at INMED and the increasing opportunities of funding for the hosting of clinicians in basic research institutes at different stages of their career.

The INMED has implemented an efficient and original management system that ensured *i)* a transparent and whenever possible collective governance and decision-making, *ii)* a good spirit and a strong cohesion within the institute, *iii)* an active participation of all staff categories in its daily life and activities, *iv)* the visibility of all the scientific staff of the unit, who can develop their own line of research in an independent manner, thereby favouring the progression of their career and contributing to the institute's attractiveness, and *v)* a remarkable capacity to anticipate the technological and conceptual evolution of the neuroscience field and, consequently, to define the forward-looking aspects of its scientific policy.

DETAILED EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous committee recommended the INMED to increase local collaborations with scientific neighbours on the Luminy campus, to take full advantage of the unique synergy offered by their proximity.

The INMED followed this recommendation through the creation of a new animal facility shared with IBDM (Institut de Biologie du Développement de Marseille) that offers several experimental facilities, including a virus injection and *in utero* electroporation lab. The INMED's teams have ongoing collaborations with several teams from research units of the Luminy Campus, including the Center for Theoretical Physics (one collaboration funded by a Centuri postdoctoral grant), IBDM (four collaborations), LIS (Laboratoire d'Informatique & Systèmes, three collaborations) and CIPHE (Immunophenotyping centre, one collaboration). The INMED also recruited an INSERM research engineer by sharing the need with two neighbours, the UNIS (Unité de Neurobiologie des canaux Ioniques et de la Synapse) and the LAI (Adhesion and Inflammation Laboratory).

The previous committee recommended a better integration with other scientific activities in the Marseille area.

To follow this recommendation, the INMED has strengthened its interactions with local partners in such a way that it now fully benefits from all the opportunities provided by the Marseille community. The INMED led to the creation of the Centuri multi-engineering platform in 2019 and the creation of NeuroMarseille, which funded five collaborative projects between INMED and other labs in the Marseille Neuroscience community and created the conditions for the success of the Equipex Circuitphotonics bringing together INMED, INT and Institute Fresnel.

The previous committee recommended that the INMED maintain a good relationship with 'Neurochlore' (hosted by INMED) to help this company to develop independently in the near future while provisioning external space for Neurochlore to free space within INMED.

To follow this recommendation, the head of the INMED imaging facility was hired on temporary missions to help Neurochlore purchase and install new microscopes and a couple of graduate students were co-supervised between INMED and Neurochlore. Furthermore, the company moved to a new location on the campus dedicated to start-up companies, thus making space available for the new INMED recruits.

The previous committee recommended the INMED to prioritise the recruitment of additional technical and administrative staff.

To follow this recommendation, the INMED recruited nineteen non-permanent technical staff and one permanent administrative agent. One permanent INSERM optic engineer was also hired in January 2022 and an additional engineer dedicated to imaging data analysis should be recruited on a permanent position by the University in 2022.

The previous committee recommended the expansion of the animal facility

A new facility shared with IBDM until 2023 has opened in April 2021.

Overall, the INMED followed the recommendations of the previous committee.

B – EVALUATION AREAS

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

Assessment on the unit's resources

The INMED is composed of ten independent research teams that share a common scientific goal and expertise in circuit physiology, electrophysiology and anatomical approaches, but develop complementary experimental strategies covering the full spectrum of brain description from molecules to behaviour. The human resources and expertise present in the teams are well balanced and in a perfect match with the institute's objectives. The technological environment is outstanding, with a leading position of the institute in the implementation of state-of-the-art technological facilities. The unit has been very successful in securing funding with a total annual income of about 3 M€. Its administrative management is efficient and seems to be appreciated by the INMED staff. Overall, the INMED is well resourced, benefits from an outstanding technological environment and is efficiently administered.

Assessment on the scientific objectives of the unit

The INMED pursues a well-focused objective dedicated to the understanding of the circuit-level of the plasticity mechanisms that operate during brain development, learning and neurodevelopmental/neurodegenerative disorders. This research objective provides the INMED an original positioning, makes it very attractive and contributes to its high national and international visibility. To achieve this goal, the INMED has perfectly anticipated the evolution of neuroscience research towards more integrated experimental approaches mostly based on the use of *in vivo* imaging in combination with electrophysiology. The institute has obtained all the necessary funding to implement the requested state-of-the-art technologies.

Assessment on the functioning of the unit

The INMED has implemented an efficient management structure composed of the 'Board of Directors' that gathers every month the team leaders and the administrative officer and is the central place of decision-making on any strategic question, the Unit Council, a consultative body composed of both elected and nominated members that meets four times a year and provide advice on the budget, lab organisation and recruitment of new staff, and four-line managers who assist the director in all issues regarding space allocation, infrastructure, equipment, etc. Most important decisions are taken in a transparent and whenever possible collective manner and seem to be well accepted by the staff of the unit.

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

Strengths and possibilities linked to the context

The research activity at INMED is performed within ten research teams that share a common scientific goal and, for most of them, a common expertise in circuit physiology, molecular or anatomical approaches, and electrophysiology. The strength of the INMED project is its ability to bridge the gap between early developmental processes and circuit physiology and dysfunction in the adult brain from behaving animals at the mesoscale level. Such a dual and systems-based approach is quite unique worldwide and provides the INMED an original positioning in France and abroad, where neurodevelopment and circuit neurophysiology are most often investigated separately.

The INMED projects are supported by five technological platforms. Four of them are hosted at INMED:

- i) the 'Animed' animal facility that is in the process of moving to a new building located on the campus, allowing increasing capacities (~500 m², 3 300 cages), higher housing standards as well as new experimental services such as virus injections and *in utero* electroporation;
- ii) the testing facility allowing assessment of motor, mood and cognitive functions in pre-clinical models;
- iii) the InMagiC imaging facility which has recently integrated France Bio Imaging and PICsL, a structure that gathers the main Luminy imaging facilities (IBDM, CIML, IMM and INMED) and got the IBISA label;
- iv) the PBMC (Molecular and Cellular Biology platform) that provides service for outsourced single-cell transcriptomics and brain organoids and offers on-demand genotyping. In addition, the INMED benefits from the multi-engineering platform of the Turing Center (Centuri) that offers services in mechatronics, bioinformatics, data mining and curation, optics instrumentation.

The INMED has established a strong relationship with the neurology, neurosurgery and paediatrics departments of Marseille University hospitals and is a founding member of the FHU Epinext and DHUNE.

Over the evaluation period, the INMED has markedly strengthened its interactions with the local neuroscience community through the creation of NeuroMarseille, which gathers nine research institutes and ~3,000 people, and the creation of the graduate school in neuroscience NeuroSchool. The INMED has played a leading role in the creation of these structures that strongly contribute to the visibility and attractiveness of the institute.

Weaknesses and risks linked to the context

Although the human resources and technical skills present in the teams are evenly distributed and generally adapted to the teams' projects, several teams do not benefit from the technical support of a tenured technician/engineer to ensure the important function of the lab manager.

Overall, there is a deficit of tenured technical staff not only inside certain teams, but also in some platforms, which can be detrimental to the projects of the unit and its teams on the long term.

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

Strengths and possibilities linked to the context

The INMED project is highly relevant and relies on an original strategy to allow analysis of the developmental timeline of the circuit dysfunction in neurodevelopmental disorders so that its objectives cannot be meaningfully and successfully approached by many institutions worldwide. They address important societal challenges such as a better understanding of the pathophysiological mechanisms underlying intractable neuropsychiatric disorders possibly linked to abnormalities of neurodevelopment, such as epilepsy, intellectual disability, autism spectrum disorders and schizophrenia.

To achieve its goals, the INMED has shown an impressive capacity to anticipate the evolution of neuroscience research towards more integrated experimental approaches, largely based on the use of *in vivo* imaging and electrophysiology. Such approaches generate an increasing amount of data and thus require novel skills in data mining and curation as well as infrastructure for data storage.

During the reporting period, the INMED has further expanded innovative, large-scale, quantitative experimental approaches to describe brain functions at circuit level by several actions:

- i) the development of cutting-edge imaging approaches that culminated in the creation of the Circuitphotonics platform,
- ii) its integration in the Centuri community and the recruitment of theoretical neuroscientists,
- iii) and the recruitment of PIs with a systems neuroscience background.

The INMED has implemented a clear decisional structure to define

- i) its research policy and scientific objectives, the exploitation of its findings, and the organisation it implies (e.g. recruitment of new team leaders);
- ii) the functioning, evolution and budget of the common platforms and services of the unit
- iii) and the creation of new facilities based on users' needs.

Regarding the forward-looking aspects of its policy, the INMED has been proactive and defined during a retreat of its PIs five major challenges that will be collectively explored by several teams in the future years, namely

- i) the polarity of GABAergic transmission in development and disease;
- ii) the identification of early functional or behavioural signs of Alzheimer's disease;
- iii) the characterisation of key developmental sequences affected in autism spectrum disorders;
- iv) the contribution of the balance between self-referenced and world-driven neuronal representations to the formation of cognitive maps
- v) and the identification of anatomo-physiological determinants of circuit dysfunction in epilepsy and associated comorbidities.

Weaknesses and risks linked to the context

There is no weakness or risk identified in the INMED scientific strategy.

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

Strengths and possibilities linked to the context

The INMED has implemented an efficient and participatory management that mainly relies on the 'Board of Directors' where most if not all strategic decisions are made transparently (minutes of each meeting are sent by email to all the unit's staff within the next fifteen days following the meeting). The same transparent procedure is applied for the minutes of the unit's councils.

The INMED is highly respectful about gender equality and was amongst the first signatories of the Alba declaration on equity and inclusion (<https://www.alba.network/declaration>). Accordingly, gender equality is respected for the composition of INMED committees and recruitment. Women are present in leadership

positions: the unit's director is a woman, three teams out of ten are directed by women and two are co-directed by women and men. The ten teams that will apply for the next contract will be gender balanced (5 men, 5 women PIs). Furthermore, a committee for gender equality composed of the different staff categories has been created to follow and improve gender equality in the unit.

The INMED pays particular attention to 'non-francophone' staff through writing all administrative and scientific communications (general emails, INMED internal rules booklet, newcomer booklet, minutes from the Board of Directors and Unit Councils) in French and English. Internal seminars are preferentially given in English. The INMED is also attentive to the working conditions of its personnel, safety, and the prevention of risks inherent to animal experimentation (formations paid by the unit to all staff, including PhD students), virus handling and human material manipulations (extension of the L2 laboratory, replacement of its ventilation system...), and fire (fire drills are organized once or twice a year and reports are made to the INMED staff with aspects to improve). Regarding psychosocial risks, the INMED has created a dedicated working group gathering all staff categories, which performs anonymous surveys that are analysed by Inserm, proposes solutions to the items identified as problematic from these surveys and ensures the implementation and follow-up of the proposed solutions. The INMED is aware of the efforts to be made for environmental preservation and has created the GreenMed working group in charge of organising educational actions regarding the environmental footprint of the unit's research activities, and to propose measures to reduce it. Amongst measures taken by the unit, one can quote the optimisation of the heating and lighting systems, favouring travelling by train, videoconferences and teleworking whenever possible, and the reduction of plastic wastes from research activities. The INMED has taken all the necessary measures for the protection of scientific data and the security of its computer systems. Experiments are registered in laboratory notebooks to ensure monitoring and protection of experimental results. The notebooks have an identification number and are kept by INMED after staff departures. The protection of information and computer systems at INMED follows the guidelines of Inserm regarding information systems security policy (PSSI) and of the GIP Renater charter. The INMED network is connected to the Inserm institutional firewall, and the Aix-Marseille University network equipped with a range of network security devices.

Weaknesses and risks linked to the context

Although there is no major weakness of the unit regarding human resources management, safety, sustained development, and the protection of scientific assets, all the data storage systems seem to be located within the INMED building with currently no remote backup in another building. The unit has not yet implemented an electronic lab book that provides better traceability and security than the traditional lab books distributed by institutions.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The INMED has an outstanding scientific reputation and is highly attractive at both national and international levels. The unit was able to attract thirteen new permanent researchers/engineers and one new group leader from a prestigious institution (Crick institute), thus expanding the skills available at the institute. The INMED members gave more than 200 invited conferences over the reporting period, including plenary lectures at the most important international meetings in the field of Neuroscience (e.g. SFN and FENS meetings). They received prestigious awards and actively participated in the scientific committees of national and international scientific foundations and institutions, thereby contributing to the construction of European and international Neuroscience research.

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 INMED scientists have given more than 200 invited presentations during the reporting period, including plenary lectures at major Neuroscience meetings such as SFN or FENS meetings. They have organised twenty international meetings and symposiums at international congresses and have been part of thirteen scientific committees for meeting organisations. They hold editorial responsibilities in 27 international journals, including reputed generalist (e.g. Elife, Plos Biology, Journal of Human Genetics) or neuroscience-specialised journals (e.g. Journal of Neuroscience, Cerebral Cortex, Hippocampus, eNeuro, Neuroscience...). They take part in local (Centuri steering and engineering committees, Marseille Neuroschool, UFR science Marseille), national (scientific panels of INSERM, CNRS and ANR, committees of ten foundations, including the Fyssen, Bettencourt-Schueller,

FRC, FFRE, LFCE, MARMARA, APAC, Prader-Willy and Lejeune foundations) and international (European Academy of Science, EMBO, Schlumberger foundation, Wellcome Trust, Swedish research councils, Norwegian research councils, FNRS (Belgium), Brain Allen Science Advisory Board, NIH, etc.) scientific committees. Members of the INMED have directorship responsibilities at the university level (Vice-Dean Recherche of the Aix-Marseille University, direction of the Doctoral School in Biology and Health, direction of the Biology Department). One INMED PI is the president of the Neuroscience Inserm scientific committee. She is also a member of the ITMO Neuroscience experts together with the unit's director. The INMED staff won various international, European, and national scientific prizes and awards. The unit director was awarded the CNRS silver medal, the Bettencourt Life Sciences Prize, the Spoelberch foundation prize, the Allianz foundation prize, Institut de France prize and the FRM Brixham Prize. Other INMED scientists were awarded the Scientific Innovation Prize from the French Academy of Sciences, the Innovation Prize from Inserm, the Young Researcher Prize from the Bettencourt-Schueller Foundation, the Australian Neuroscience Society Paxinos-Watson award for the best research article in Neuroscience. One INMED associate professor was elected junior member of IUF (Institut Universitaire de France).

Weaknesses and risks linked to the context

There is no major weakness regarding the attractiveness of the unit, but scientific recognition and awards could be better shared amongst all scientists of the institute.

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

Strengths and possibilities linked to the context

During the reporting period, the unit recruited five junior researchers, one study engineer and one research engineer through national competitions. Furthermore, it attracted eight established researchers (4 CRCN, 2 MCU, 1 PUPH, 1 DR2) and eleven engineers from other national laboratories. Most importantly, it recruited a new PI from a prestigious institution (Crick Institute in London) with a multidisciplinary expertise complementary to those present in existing teams through a call launched in the frame of the Chair of Excellence Initiative of the Aix-Marseille University. The INMED is also part of a new PI call launched in 2022 in the frame of Centuri to recruit a computational neuroscientist and has already received several outstanding applications from junior and senior researchers working in renown institutions (ENS Paris, Janelia Research Campus USA). The newly recruited tenured scientists rapidly adapted to their novel environment, have been successful in a grant application and actively participate in the collective life of the institute, thus demonstrating the quality of the INMED staff hosting policy. The INMED also hired 70 PhD students and 47 postdocs during the reporting period. At the start of their contract, PhD students and postdocs follow several courses on security issues, good ethical practice in research and benefit from a dedicated day to learn all about the institute (general services, technical platforms, etc.). They also follow the PhD program of Neuroschool that regularly organises scientific days where PhD students can present their work in the form of posters or short talks. Within the INMED, PhD students and postdocs are involved in external seminar organisation. They can propose a list of external speakers who are invited to give seminars. They organise a dedicated lunch with each speaker during which they have the opportunity to ask all the questions they want without the risk of being judged by senior researchers. They are trained to give talks during lab meetings and journal clubs organised within each team and the data clubs organised at the level of the institute. Several PhD students have obtained prizes in recognition of their work, such as the thesis prize of the French Neuroscience Society, the 'prix jeune chercheur' of the Fondation Bettencourt-Schueller, underscoring the quality of research training provided at INMED. The unit regularly hosts renowned visiting researchers from prestigious institutions or universities. For instance, the INMED is currently hosting an assistant professor from Cornell University and a full professor in computational neuroscience from the University of Washington. Finally, the INMED is attentive to the 'non-francophone' community and all newcomers receive a newcomer's booklet (in French and English) available on the institute's intranet site and are informed of the INMED's rule during newcomer sessions.

Weaknesses and risks linked to the context

Women remain underrepresented at INMED, especially amongst researchers with tenure-track positions, but the INMED direction makes a real effort to respect gender equality in the institute and to facilitate the career of female researchers.

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

Strengths and possibilities linked to the context

The capacity of INMED to raise funding in response to competitive calls from French, European and foreign institutions is outstanding. In addition to the eleven previously obtained European grants that ran over the reporting period (including 2 ERC Consolidator, 1 ERC Starting and two FP7 HEALTH projects, for a total granted amount of 7,795 k€), the INMED obtained a new ERC Synergy grant (3 M€ funding for the Institute) and twelve new international grants (for a total of 1,722 k€), in addition to new European projects (ERA-NET, E-RARE, COFUND, Human Brain Project, European Neighbourhood Instrument and Marie Skłodowska-Curie Individual Fellowships, for a total of 1,601 k€). Twenty new projects were funded by the National Research Agency, for a total of 4,064 k€ in addition to the seventeen projects running from the previous period. The INMED was also awarded 40 novel grants for a total amount of 2,522 k€ over the reporting period. The INMED has also been extremely successful in raising funding dedicated to equipment from local organisations (411 k€ obtained from the Région PACA) and Future Investments Programmes (PIA). The unit's director obtained a 4,265 k€ funding dedicated to innovative imaging technologies to be implemented on the Circuitphotonics centre, a platform co-managed by INMED, Institut des Neurosciences de la Timone and Institut Fresnel, in response to the PIA call Equipements Structurants pour la Recherche (ESR/EquipEx+).

Weaknesses and risks linked to the context

There is no weakness identified in the capacity of INMED to raise funding from many sources in France and abroad.

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

Strengths and possibilities linked to the context

As already mentioned, the research made at INMED is supported by in-house technological platforms equipped with cutting-edge technologies and the multi-engineering platform of the Turing Center (Centuri) that provides expertise in mechatronics, bioinformatics, data mining and curation as well as optics instrumentation. Most of these platforms are handled by permanent technical staff who can provide users with technical support and services and are also trained in management and administrative issues. Amongst the major equipment acquired over the reporting period, one can quote hoods, ventilation units, CO2 system and a chemical lock system implemented in the new animal facility, three Inscopix miniscopes, one Bruker two-photon microscope, one custom-made all-optical systems (holography and two photons) and one virtual reality set-up. All in all, the cutting-edge equipment available in the INMED teams or the platforms hosted by the institute markedly contribute to the INMED attractiveness over the world.

Weaknesses and risks linked to the context

There are no major weaknesses or risks identified regarding the equipment available at INMED, but some platforms still lack permanent technical staff to maintain an optimal service and a high level of technological development so that they can continue to offer their users solutions at the highest international standards.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The scientific production of INMED is outstanding in the quantitative and qualitative points of view. The unit published around 300 articles or reviews during the reporting period. The scientific quality of the research performed in the institute is demonstrated by the large number of publications in wide readership and historically recognised journals specialised in Neuroscience with high quality standard requirements and revision processes, such as Science, Nature Neuroscience, Nature Communications, Neuron, Brain, Molecular Psychiatry, Elife, Cell Report, etc. Notably, 36% of INMED publications involve several teams of the unit and each team has a minimum of four publications shared with other INMED teams. This is remarkable and reflects a strong commitment of all teams in the scientific policy and objectives of the institute. The INMED must be congratulated for this. Furthermore, the scientific production of the unit is shared out in a balanced manner between the teams, involves all tenure scientists and complies with the guidelines of the INMED institutions regarding integrity, ethics and open science.

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

Strengths and possibilities linked to the context

The scientific quality of the research performed at INMED is assessed by the large number of publications in wide readership and historically recognised journals specialised in Neuroscience with high quality standard requirements and revision processes. Amongst others, one can quote Science, Nature Neuroscience, Neuron (4 articles published during the reporting period), Nature Communications (6 articles), Brain (2 articles), Molecular Psychiatry (6 articles), Elife (12 articles), Cell Report (5 articles), PNAS (4 articles), Journal of Clinical investigation (2 articles) and Cerebral Cortex (20 articles). The scientific quality of the research performed at INMED is also demonstrated by the large number of invited conferences given by the INMED researchers/professors (220 over the reporting period) and their successful applications to highly competitive national and international calls.

Weaknesses and risks linked to the context

There is no weakness identified regarding the quality of the scientific production of INMED.

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

The INMED produced an impressive number of publications during the reporting period, including 260 original articles, 41 review articles, 59 meeting abstracts and ten book chapters. This represents a median number of 38 articles/reviews per team, with four teams exceeding the median publication rate of the unit, indicating that the scientific production is well balanced between the teams. A strength of INMED is the high proportion of multi-team publications (36% with at least 2 co-authors from 2 distinct teams contributing to the article/review). This represents a median number of 22 multi-team articles per team and each team has published with at least four other INMED teams. This outlines the synergy between the INMED teams and their strong commitment in the INMED scientific project. The scientific production is also shared out in a balanced manner between the INMED scientists. Most if not all, tenured researchers and professors contributed to the scientific production of each team with at least one article signed in a position of responsibility published over the reporting period. The policy of INMED is that all PhD students and postdoctoral fellows trained at INMED have at least one publication often as a first or equally-first author before the end of their contract. This has been the case for the large majority of them during the evaluation period.

Weaknesses and risks linked to the context

There is no weakness identified regarding the scientific production of INMED and how it is shared between the INMED scientists.

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

Strengths and possibilities linked to the context

The scientific production of the unit complies with the principles of research integrity, ethics and open science defined by Inserm. The INMED members are committed to comply with legislative and regulatory requirements, conduct their research reliably, responsibly, and impartially both inside the institution and internationally while participating in collaborative work, and communicate with respect of intellectual property rights. Any suspicion of research misconduct at INMED is reported to the department for scientific integrity of Inserm. In addition to the authorship principles stated in the French charter for Research Integrity, the INMED has recently released a document providing its own guidelines about authorship, which must be based on an explicit role in the work carried out and outlines that all staff, including platform staff, having fulfilled such a role should be authors of the publications. Regarding the use of animals, the INMED complies with the ethical principles of the 3Rs and has created an animal well-being committee to promote animal welfare. All research projects involving animals are performed providing that an authorisation is delivered after positive ethical evaluation by animal ethics committees and final approval by the French Ministry for Research. Regarding open science and consistent with the guidelines of its institutions, the INMED teams deposit their open archives on HAL French open access repository portal (52% of INMED articles published during the reporting period). In line with the recognition by

Inserm of preprints as a form of scientific communication, the INMED teams have deposited a total of 28 bioRxiv or PsyArXiv preprints prior to their submission to peer-reviewed journals. Furthermore, one third of INMED teams have made available Matlab or Python pipelines, as well as raw data through open access repositories such as GitLab.

Weaknesses and risks linked to the context

There is no weakness or risk identified regarding research integrity, ethics and open science at INMED.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

Overall, the inclusion of the unit's research in society is excellent. The INMED has significant interactions with the University Hospital of Marseille, and other hospitals outside Marseille, is strongly supported by charities (> 3.5 M€ collected during the reporting period) and has developed regular interactions with several patient associations. The interactions with the socio-economic world are sparser and only concern a few teams, but five out of the seven patents filled by the unit during the reporting period have been licensed by start-up companies, including a start-up company founded by one of the INMED team leaders that has further been acquired by a leader company in the field of gene therapy. The INMED scientific staff are strongly committed in scientific knowledge diffusion to the lay public, with impressive diversity and originality of science outreach activities.

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

Strengths and possibilities linked to the context

Capitalising on the translational potential of its research projects, INMED has developed longstanding collaborations with clinicians of the University Hospital La Timone, and other hospitals outside Marseille. The INMED is one of the founding institutes of the FHUs Epinext and DHUNE and continues to develop privileged interactions with the Neurology, Neurosurgery and Pediatrics Departments of the Hospital la Timone. The interaction of INMED with the clinics is facilitated by the fact that the INMED hosts several medical doctors (four during the next contract) from AP-HM (and AP-HP). Further, the institute hosted medical interns on several occasions and will launch a summer school for medical students in 2023. The institute is strongly supported by numerous charities (FRM, FRC, Fondation Lejeune, Fondation de France, ARSEP, Ligue contre le Cancer, ARC, Gueules Cassées etc.) for a total amount of 3.6 M€ over the reporting period. INMED has also developed a strong relationship with some patient associations (e.g. organisation of the ARSEP open lab day dedicated to multiple sclerosis patients in 2019 and 2021).

Weaknesses and risks linked to the context

There is no weakness or risk identified regarding the non-academic interactions of INMED.

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

Strengths and possibilities linked to the context

In collaboration with a laboratory of Bordeaux, one INMED team provided evidence of the therapeutic potential of gene therapy targeting GluK2 kainate receptor in patients with drug-resistant temporal lobe epilepsy (TLE). These findings have led to the filing of four patents licensed to Corlieve Therapeutics, a start-up company founded by the team leader with two other scientists in 2019. The discovery that an engineered miRNA targeting the mRNA encoding GluK2 suppresses both spontaneous recurrent seizures in chronic epileptic pre-clinical model and epileptiform discharges in organotypic hippocampal slices surgically resected from patients with drug-resistant TLE has led to the selection of a lead compound that is currently entering scale-up and safety testing prior to initiating a clinical study in patients with drug-resistant TLE. Based on this progress, Corlieve Therapeutics was acquired by UniQure, a leader company in gene therapy (<http://uniqure.com/>). Corlieve Therapeutics is now pursuing the development of the treatment as a subsidiary of UniQure. This success story, which is lined with the creation of another company by a former director of INMED (Neurochlore, hosted by the INMED until the end of 2017), outlines the valorisation potential of the research made at INMED and should

encourage the other teams of the institute to promote the valorisation of their results. The unit filed a patent on the ability of peripheral oxytocin administration during the first week of life to restore a normal feeding behaviour in neonates and social behaviour and cognition up to adulthood in Prader-willy syndrome. Three companies have got a licence to exploit this patent. Two industrial contracts have also been obtained by another INMED team (one with AstraZeneca and one with Axonis Therapeutics). One team has established a partnership with 'Inscopix', an expert company in miniscope-mediated calcium imaging in freely behaving animals.

Weaknesses and risks linked to the context

Only a minority of INMED teams have filled patents over the reporting period and four out of seven patents were filed by the same team. Despite the success story of the creation of Corlieve Therapeutics and its acquisition by UniQure, the relations of INMED with industry remain sparse and might certainly be reinforced in view of the quality of the research made by the institute, its potential for identifying new therapeutic targets in currently intractable neurodevelopmental diseases and the international visibility of the institute.

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

Strengths and possibilities linked to the context

The INMED has been hosting for many years a highly original and successful platform dedicated to science outreach for high school kids, medical school interns and patient associations (e.g. the ARSEP open lab day dedicated to multiple sclerosis patients in 2019 and 2021). This platform, called 'Tous chercheurs', is unique in France and regularly organises practical courses to raise public awareness of science and technology. The 'Tous chercheurs' platform will launch a summer school for medical students in 2023 and aims at enlarging its opening to a wider public, for example through the training of journalists to research. The INMED staff are involved in the organisation of events dedicated to the lay public, such as 'la Nuit des chercheurs' and 'La Semaine du Cerveau' in Marseille and its region, give lay audience conferences, take part in debates in society and make interventions in several educational frameworks such as 'La Maison des apprentis'. Some of them participated in an artistic show that explains the perception of music and movement and in a short theatre play that explains the role of the striatum dysfunction in Parkinson's disease and the dilemma between exploring new ideas versus exploiting technology. This theatre play consists in a written dialogue between an INMED PI and a professional actor, followed by an exchange with the public. One INMED researcher created a MOOC (Massive Open Online Course) at Aix-Marseille Université in 2020 (<https://www.fun-mooc.fr/en/cours/autour-des-neurones-focus-sur-la-myeline/>). One team participated in a video broadcast on YouTube to explain its research to a general audience with more than 1,700 views (<https://www.youtube.com/watch?v=cdvftDz2w6k>). The team has a Twitter account (700 followers) to highlight research performed in the team and elsewhere. All these examples illustrate the strong commitment of the INMED and its personnel in scientific knowledge diffusion to the lay public and the diversity and originality of its science outreach activities.

Weaknesses and risks linked to the context

There is no weakness in knowledge diffusion to the lay public at INMED.

C – RECOMMENDATIONS TO THE UNIT

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

The committee recommends the INMED to strengthen its interactions with the clinics given the high translational potential of its research. It thus recommends that the institute attract clinicians at the different stages of their career by applying to fellowships for medical students (e.g. FRM and Inserm fellowships) and considering a new opportunity to attract hospital practitioners' holder of a PhD on Inserm 'DR-PH' positions. It also recommends the INMED to pursue its efforts to recruit tenured engineers to manage the technological platforms and ensure the formation and supervision of their users, especially PhD students and postdocs. The committee endorses the INMED strategy to mutualise technical staff between platforms and teams given the current policy of institutions regarding technical staff allocation but recommends that the INMED management team precisely defines in the job description of the staff their function and the sharing of their time between the teams and the platforms. The committee also recommends improving internal mentoring of technical staff to help them progress in their career by creating a structure comprising researchers and engineers in charge of reviewing the applications of candidates to promotions.

Recommendations regarding the Evaluation Area 2: Attractiveness

As mentioned above, the committee recommends the INMED to strengthen its attractiveness towards medical students and hospital practitioners by applying to dedicated fellowships and positions to promote translational research within the institute and increase its interactions with Marseille University hospitals and hospitals from other regions.

Recommendations regarding Evaluation Area 3: Scientific Production

The committee has no specific recommendation regarding the scientific production of INMED which is outstanding, even though certain teams should pursue their efforts to publish in higher impact journals.

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

The committee recommends the INMED to capitalise on its past successes such as the Corlieve success story to encourage all the teams to promote the valorisation of their own results by filing patents, and to strengthen their relations with industry, in view of the quality of the research made by the institute and its potential for identifying new therapeutic targets in currently intractable neurodevelopmental diseases. The INMED should also take advantage of the programs implemented by the Aix-Marseille University to promote partnerships between academic research institutes and industry and apply to the dedicated calls.

RESPONSES TO SUPERVISING BODIES CONCERNS (IF ANY)

TEAM-BY-TEAM ASSESSMENT

Team 1: Cortical development
 Name of the supervisor: Carlos CARDOSO

THEMES OF THE TEAM

The team explores the cellular and molecular mechanisms involved in the pathophysiology of neurodevelopmental disorders including cortical malformations, epilepsy, intellectual disability, or autism spectrum disorders. Two major objectives are (i) to identify cells autonomous and non-cell autonomous mechanisms that control migration and maturation of cortical neurons and (ii) to characterise the seizure-generating zone, at the structural and functional levels. The team uses a wide range of multi-level analyses that include multi-omics, immune phenotyping, viral tract tracing, electrophysiology. The team has also translational research objectives with strong links with French and international clinicians.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The Team has positively addressed important concerns raised in the last evaluation. First, it has reinforced its task force with the integration of two tenured researchers and one Inserm Research engineer. It has also significantly increased the number of PhD students (7). Second, both senior and junior Team members will focus on ambitious, coherent and well-structured projects for the future period. Third, the Team is developing active and strategic collaborations with other INMED teams and with highly visible, outstanding international groups. These new synergies will open new research avenues (via sharing and extending concepts and approaches) which will undoubtedly facilitate the successful completion of the proposed projects. The Team presently includes seven PhD students and three postdocs. During the past period, all early-stage career members (PhD students and postdocs) have published at least one paper in excellent journals (Mol Psy, Nat Comm, etc.) as the first author, ensuring their international visibility.

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	3
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	2
Subtotal permanent personnel in active employment	7
Non-permanent teacher researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	1
Post-docs	2
PhD Students	5
Subtotal non-permanent personnel	8
Total	15

EVALUATION

Overall assessment of the team

The Team gathers an excellent combination of complementary expertise in basic research and has developed innovative models and approaches. It has strong and fruitful links with renowned clinicians and pathologists via European networks (ERA-NET). The level of national and European funding is excellent. The Team scientific productivity is excellent and internationally competitive. It includes seventeen articles out of which eight are in high-level journals, six clinical articles and three reviews or editing topics. The team members are invited in prestigious meetings and institutes (MPI, Weizmann, etc.).

Strengths and Possibilities linked to the context

The team greatly benefits from the rich INMED environment with outstanding innovative facilities and membership of the Neuromarseille Institute and the Marseille Imaging Institute. The Team's members share common scientific objectives and bring complementary experimental know-how, bridging the gap between neurobiology, anatomy, cell and molecular biology, and genetics. Via intra-INMED collaborations, the Team also has access to state-of-the-art electrophysiology explorations. The innovative pre-clinical models and approaches established by the Team constitute very strong assets for the successful implementation of the future projects. In addition, strategic international collaborations with top labs have been established, which will significantly extend the Team's expertise and capacities to implement state-of-the-art omics approaches, biochemistry and *in vivo* electrophysiology. The team is a member of an outstanding European clinical network (ERA-Net, Neuromig) that is at the front of excellence. This strong link with renowned clinicians provides access to clinical data, brain tissue and genetic information, and therefore significantly enrich the Team's lines of investigation. These collaborations will ensure successful translatability of basic research findings into the clinic and therefore reinforce the Team's international visibility and competitiveness. New opportunities are developed by the Team as it is engaging novel collaborations with nonacademic industrial partners which paves the way for recording neural activity in deep brain regions in a naturalistic environment and for developing novel *in vivo* brain-delivery procedures.

Weaknesses and risks linked to the context

The Team workforce and know-how are likely to decrease when the two Emeritus and the senior DR1 will eventually retire. However, this can be anticipated by a well-planned scientific handover and mentoring of the Team members of the emeritus. The Team benefits from limited technical support (0.5 Research study Engineer), which appears very low with respect of the variety of projects and techniques implemented by the Team. Institutional support for technical staff is weak which could constitute a risk/threat for maintaining optimal Teams' activity.

RECOMMENDATIONS TO THE TEAM

Joining forces with microglia experts might be useful regarding the CMV-related pathogenesis project. The Team should reinforce its positive and dynamic trajectory. The Team might envisage funding technical staff on its grants to provide efficient technical help to the different projects. While the contribution of the Emeritus Directors of Research is highly invaluable, their activity is unfortunately hindered by administrative limitations. The team should therefore actively seek to recruit or attract new tenured Inserm researchers to strengthen its workforce and capacities to appoint future PhD students and exert administrative responsibilities (grants, etc.). It should also anticipate the eventual retirement of the emeritus.

Team 2: DEVELOPMENTAL SCAFFOLDING OF ADULT HIPPOCAMPAL CIRCUITS

Name of the supervisor: Rosa COSSART

THEMES OF THE TEAM

The team addresses key questions on the formation, maturation, and function of hippocampal and neocortical circuits. Its main objectives are to unravel how development shapes adult cortical circuits, how these circuits define cortical dynamics and how patterns of these dynamics change over time. It combines multiple approaches such as in vivo imaging, electrophysiology, anatomy, genetics, and theoretical analyses. In close relation to its research topics, the team is also involved in the development of advanced multiphoton imaging techniques and has established different outstanding collaborations and partnerships with researchers and imaging platforms. Finally, it has developed several signal processing methods that are freely available to the community in gitlab.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team responds positively to all the recommendations made in the previous HCERES report. Firstly, it strengthened its links with computational and theoretical neuroscientists by establishing five new collaborations. Secondly, the strategic position of the team at INMED has allowed it to further increase its visibility (and that of the institute) as evidenced by the number of prestigious awards and invitations obtained by the PI and some other members. Finally, it also strengthened its interaction with other local structures by leading several strategic plans (e.g. Circuitphotonics platform) and organising international meetings (e.g. The Fresh look on inhibition) in Marseille.

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	3
PhD Students	6
Subtotal non-permanent personnel	10
Total	15

EVALUATION

Overall assessment of the team

The scientific production and technical achievements of the team are outstanding. The team has published remarkable work on cortical circuit assembly and function *in vivo* in highest-level journals such as *Science*, *Neuron* or *Nat Commun*. The fundraising is also impressive; the team has previously and recently obtained a strong financial support from competitive local, national, and international institutions and, as such, the development of the projects in the following years is secure. Overall, the team has a very high international reputation and appeal.

Strengths and Possibilities linked to the context

This team has been very successful at all levels over the last six years. Scientifically, it has a longstanding expertise in neurodevelopment and neurophysiology, and continues to make significant contributions in these fields. It has been a pioneer in deciphering the dynamics of neuronal ensembles *in vivo*, both early in development and during adulthood. The team is also at the forefront of technological developments in multiphoton microscopy for *in vivo* imaging and has received significant funding to pursue this line of research (ERC Synergy, Equipex). The four permanent researchers of the team have different but complementary expertise, which constitutes an added value for developing new strategies to analyse the maturation and function of neural networks. Of note, the team has also succeeded in recruiting two young scientists through national competition; one of them left the academia and is the CEO of Unistellar company. In addition, PhD students and postdocs publish in high quality journals and have received prestigious prizes early in their careers. The team participates in the organisation of international scientific meetings in Marseille as well as in outreach activities in schools and during the French Brain Awareness week (La Semaine du Cerveau). It also maintains close links or is an active partner of Centuri Multi-Engineering and Circuitphotonics platforms in Marseille. In summary, this is an outstanding team and, as a meritorious consequence of its recognition, it plays a leading role in the institute and the development of Neuroscience in Marseille.

Weaknesses and risks linked to the context

There are no weaknesses for this team.

RECOMMENDATIONS TO THE TEAM

As suggested in the team's report, the hope of developing collaborative projects with industry and clinicians is an excellent idea and is strongly encouraged.

Team 3: Neuronal coding and plasticity in epilepsy

Name of the supervisor: Valérie CREPEL

THEMES OF THE TEAM

The team has a strong expertise in the pathophysiological mechanisms of epilepsy with a special focus on the action of glutamatergic receptors, mainly kainate receptors. It uses *ex vivo* and *in vivo* electrophysiological recordings and immunostainings in old and new pre-clinical models of epilepsy. With the recent arrival of a senior researcher, the team is also interested in the role of adhesion molecules and associated K⁺ channels in regulating neuronal excitability and myelination as potential critical elements in epileptogenesis. Besides, the PI of the team has obtained the financial support to create a start-up aiming at developing new therapies for drug-resistant epilepsies by targeting epileptogenic receptors.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team positively responds to the recommendations made in the previous HCERES report. It collaborated with two clinicians in Marseille, with whom it has a submitted publication. Notably, three international patents were delivered during the present period and the start-up, Corlieve, was created with the help of Inserm-Transfert. The start-up was recently acquired by UniQure. The team leader also obtained an international Era-Net Neuron grant and participated as a collaborator in some projects of other teams at the institute. Finally, it recently recruited a senior and a young researcher with permanent positions which will strongly increase the forces 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	1
Non-permanent research supporting personnel (PAR)	2
Post-docs	1
PhD Students	3
Subtotal non-permanent personnel	7
Total	11

EVALUATION

Overall assessment of the team

The expertise of the team in elucidating the mechanisms leading to different epilepsies is very valuable and has strong translational potential. In addition to its excellent scientific activity, the team is actively involved in R&D research. Notably, the team has contributed to the creation of the Corlieve start-up, now owned by UniQure, to develop a novel strategy for the treatment of temporal lobe epilepsy. As recognition of its work, the team leader recently received the prestigious INSERM Innovation award.

Strengths and Possibilities linked to the context

This team has strong expertise in the physiopathology of epilepsies, on the mechanisms triggering epileptic seizures via ionotropic receptors. A major contribution has been to the identification of these receptors as potentially interesting therapeutic targets. With the creation of the start-up Corlieve in 2019, the team has developed a clear strategy to directly exploit its results, adding strong translational value to its research. Indeed, several patents resulting from the team's work have been filled. The recent recruitment of two researchers with permanent positions (a senior and a young researcher) as well as that of technical staff greatly strengthened the forces of the team. In addition, PhD students have been published, and some other publications resulted from the collaboration with other teams at INMED. Therefore, the team has very good interaction with other teams at the institute. Overall, its development dynamic is very positive.

Weaknesses and risks linked to the context

There are no major weaknesses for this team.

RECOMMENDATIONS TO THE TEAM

To maintain and further enhance the visibility of the team in the competitive international epilepsy community, a recommendation might be that all members focus their work on the most promising lines of research. Although it regularly publishes interesting work on epilepsy, it would also be important to target more prestigious journals to help the career development of young researchers.

Team 4: Neuronal coding of space and memory

Name of the supervisor: Jérôme EPSZTEIN

THEMES OF THE TEAM

The team has a longstanding expertise in the field of spatial cognition associated to a comprehensive knowledge of morpho-functional properties of hippocampal networks both at the cellular and circuit levels. The team was already renowned for its expertise on the role of intrinsic excitability in spatial coding at the single cell level which was further developed at the level of population of neurons. Two additional key and original aspects of the research conducted in the team are its ability to perform a single cell as well as population cell recordings in live animals navigating under virtual reality. This experimental set-up is unique in France and allows addressing questions that cannot be studied in animals navigating in a real environment. While initially dealing mostly with spatial cognition in the normal brain, the team is now initiating collaborations to study the consequences on cell excitability of various disease-related pathological processes, either neurodegenerative or neurodevelopmental.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has positively responded to the major recommendations made in the previous HCERES report by establishing new collaborations with physicists through the CENTURI initiative and pursuing and even increasing its collective expertise in spatial cognition using virtual reality, thereby fulfilling the recommendation of pursuing an internationally competitive research. The team leader and notably his Co-PI obtained various national grants, also responding positively to the recommendation of favouring the independence of the second PI.

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	0
Scientist (Chargé de recherche, CR) and associate	2
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	0
Subtotal permanent personnel in active employment	3
Non-permanent teacher researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	0
Post-docs	1
PhD Students	4
Subtotal non-permanent personnel	5
Total	8

EVALUATION

Overall assessment of the team

The team has an outstanding expertise in spatial cognition using virtual reality, which is quite unique worldwide and is only present in this team in France. Regarding fundraising, the team has shown an excellent capacity (PI of three different ANRs). Team visibility and attractiveness are excellent, with the PI being frequently invited to give lectures in renowned institutes (ENS, UCL, Cajal Institute) and one CR joining the team. Although the team regularly publishes at a very good/excellent level of publication (2 eLife papers), the overall production remains somewhat modest.

Strengths and Possibilities linked to the context

The team has a remarkable expertise in the study of spatial coding in navigating in a virtual reality environment. Only a few teams worldwide are mastering this kind of behavioural analysis in pre-clinical models performing tasks in virtual environments while being able to simultaneously record cell excitability at either single-cell or cell-population levels. Other major and outstanding technological developments (large-scale virtual reality environment) have been initiated, which could eventually be a risk (see weaknesses and risks). All PhD students have been published as 1st authors in excellent journals. Most postdocs have also contributed to at least one publication as the principal author. Of note, one doctoral fellow was awarded the Fondation Bettencourt Schueller young research price for his PhD work.

The team has several excellent interactions materialised by joint publications with various other teams of the INMED. Besides, the team has collectively secured significant funding for the coming period (2 ANRs: SynDev as PI, Hyppodev as partner for a total of 475 keuros).

Weaknesses and risks linked to the context

Although published in good to excellent journals, the team's production remains somewhat modest. This is certainly due to the fact that, before publishing, the team had first to develop and establish very innovative methodologies and master those new tools before being able to produce, gather and interpret the huge amount of mutiparametric data generated. New technological developments recently initiated may delay the completion of certain studies conducted by the team, notably when considering that the team is engaged in questioning many (maybe too many) scientific hypotheses aiming at deciphering different processes of hippocampal coding from intrinsic cellular mechanisms up to the integrative behavioural level, and from physiological conditions to various neurodevelopmental pathological alterations.

RECOMMENDATIONS TO THE TEAM

The committee recommends that the team maintain and further enhance its visibility in the competitive international spatial coding field by publishing the very original data generated in *wide readership journals*. The committee fully supports that the team maintain a huge implication in ambitious methodological developments but recommends to carefully balance those developments with the use of these outstanding tools to address specific and focused scientific hypotheses. The committee also supports the limited investment of the team in outreach activities which was justified by its huge and strategic methodological developments.

Team 5: Early activity in the developing brain

Name of the supervisor: Roustem KHAZIPOV

THEMES OF THE TEAM

The team investigates how brain activity patterns and GABAergic transmission play a role during normal neurodevelopment as well as under different pathological conditions including neurodevelopmental disorders, epilepsy, traumatic brain injury and stroke. The team has a longstanding expertise in electrophysiological recordings in vivo, pioneering the use of intra-spinal cord silicone probes in neonatal rats. One particular aspect of the team's research is the combination of various approaches mixing in vivo electrophysiological recordings (multiple/single cell multi-electrodes array recordings) together with other sophisticated methodologies (opto and pharmacogenetics) and behavioural testing, to address the structural and functional development of the brain in anaesthetised and freely behaving animals.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The major recommendation made in the previous HCERES report was to work on maximising the synergies between the two sites of the International Laboratory, ensuring that team members from the Kazan University could better contribute to the scientific life of the INMED site. The end of the LIA contract and the recent international context has led to a refocusing of the team's activities at INMED. The increased number of permanent researchers should also help increase the team's activities at INMED in the near future.

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	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	1
Non-permanent research supporting personnel (PAR)	0
Post-docs	0
PhD Students	4
Subtotal non-permanent personnel	5
Total	12

EVALUATION

Overall assessment of the team

The team benefits from an excellent national and international recognition in its field of research. As such, the team has also been highly productive in publishing in good/excellent journals (79 articles, including more than half of them signed by the team's members in the position of responsibility). The research topics of the team rely on a large array of translational competences starting at fundamental research in neurodevelopment or inhibitory/excitatory neurotransmission and evolving towards more clinical aspects related to various disease conditions, such as neurodevelopmental disorders, epilepsy, stroke, or traumatic brain injury. Regarding fundraising, the team has shown excellent capacity with the obtaining of five consecutive ANR together with various funding emanating from local calls (NeuroSchool, Centuri, Institut Carnot) and various Foundations (Gueules Cassées, Fondation FFRE). Team visibility and attractiveness are excellent with three PIs being invited to give lectures at international symposia. The contribution to society and industry is also excellent with solid interactions with the RODDATA and Neuralynx companies to push the team's innovations to the market.

Strengths and Possibilities linked to the context

The team has a strong expertise on the role played by electrical activity in the development of the central nervous system. Its research not only contributes to significant advances in fundamental research but also finds important clinical applications. The team has produced a large number of very good scientific publications with all PIs, doctoral and postdoctoral fellows publishing during the period. The team's visibility and attractiveness are excellent with the arrival of two permanent researchers and the development of collaborations with industry (RODDATA company to further develop the phenotypix system, Neuralynx to push new devices to the market). The team has several very good interactions with many of the INMED teams as well as fruitful interactions with French (notably with hospital Necker for the sensory exploration of human neonates) and international clinicians (Charité in Berlin, Germany, Vermont in the USA), rendering their research translational by nature.

Weaknesses and risks linked to the context

A minor weakness of this team is that the presence of several PIs' makes the topics a bit scattered and disconnected from each other. It should be noted that the closing of the International Laboratory and the present international context in Europe may hamper the intrinsic capacity of communications and exchanges between the Kazan University and the scientists at INMED. The current reinforcement of the team at the INMED site should help increase the scientific excellence and attractiveness of the team, notably with new PIs recently arrived.

RECOMMENDATIONS TO THE TEAM

To maintain and further enhance the visibility of the team in the international competition, one recommendation would be to focus on the most promising research lines and to promote a better synergy between the different PIs. Communication efforts to better promote the results at the national and international level can also be envisaged. It is also advisable to promote the research themes of the two permanent researchers having MD degrees to strengthen the existing interactions with clinicians and industry and reinforce the existing translational potential of the excellent scientific developments made by the team.

Team 6: ADOLESCENCE AND DEVELOPMENTAL VULNERABILITY TO NEUROPSYCHIATRIC DISEASES

Name of the supervisor: Olivier MANZONI

THEMES OF THE TEAM

Team 6 investigates the mechanisms of development of meso-corticolimbic microcircuits and the influence of sex on these mechanisms along the first critical periods of life (including the high vulnerability of adolescence), studies how genetic and environmental insults modelling neuropsychiatric diseases affect synaptic networks and scale down behavioural working ranges and attempts to develop specific strategies to compensate these deficits in both sexes. For this purpose, the team uses a multidisciplinary approach combining electrophysiology, *in vitro* and *in vivo* imaging, quantitative neuroanatomy, optogenetics and behavioural approaches to assess the neural activities underlying behaviours, and ultimately design therapeutic protocols able to reactivate synaptic and behavioural flexibility.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The recommendations made in the previous evaluation were properly addressed.

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	1
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	2
Subtotal permanent personnel in active employment	6
Non-permanent teacher researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	2
Post-docs	1
PhD Students	1
Subtotal non-permanent personnel	4
Total	10

EVALUATION

Overall assessment of the team

Team 6 is very well funded and develops outstanding projects using state-of-the-art approaches. Its international visibility is excellent, and it develops very productive international collaborations. Its scientific production is excellent, and its training activity is remarkable. The team members are very active in interacting with the society, through classical diffusion of science to the general public and, in a more original way, through the highly innovative BestMedGrape European project aiming at developing new business opportunities and environmental sustainability.

Strengths and Possibilities linked to the context

Team 6 develops its research at the forefront of its field, and benefits from a very high national and international recognition. During the last contract period, the team made very important discoveries, including the demonstrations that 1) adolescence is a sensitive period for the emergence of cognitive deficits in response to nutritional stress, 2) perinatal cannabis exposure causes synaptic reprogramming of the developing brain and long-term behavioural deficits, 3) the deregulation of endocannabinoid long-term depression is a synaptic marker in depression and autism, and 4) the developmental trajectories of late maturing structures are sex-specific. These remarkable sets of data were obtained thanks to the combination of a broad variety of cutting-edge approaches, and published in high-profile journals (TINS, Mol. Psy., Cell Reports, Cerebral Cortex, eLife, Biol. Psy, J. Neurosci.). Overall, the output of the team is excellent: 28 peer-reviewed papers, 22 of them signed as first, last or corresponding author. The outstanding quality of Team 6 research, developed in part through productive international collaborations, allowed the team to be highly successful in obtaining numerous grants from diverse sources (International, European and French public funds, as well as funds from French Foundations) as attested by the obtainment of Grants from NIH (2 RO1 and 1 LIA together with Univ. of Indiana, USA), the EU (1 ENI 'BESTMEDGRAPE', coordinated by Univ. Cagliari), ANR (7 Grants) and several French Foundations (FRM, ARSEP, Lejeune). Between 2016 and 2021, the team has attracted six PhD students and four postdoctoral fellows who were all very productive, as they authored 26 publications during this period. Team 6 members are strongly involved in a variety of duties at the levels of INSERM (CSS4), AMU (Conseil d'UFR, Conseil Scientifique de l'UFR, Comité exécutif de la Neuroschool Neuromarseille) or Foundations (Présidence de la Société Française de Toxicologie Analytique, etc), and two of them had stays at Indiana Univ. Three members of the team are very active in citizen participatory science activities, using multiple channels including public conferences or debates (e.g., 'Controversation on Cannabis: ange ou demon'), involvement in specific events (Fête de la Science, Semaine du cerveau), radio, TV or newspaper interventions, etc. Team 6 also participates in a very original European project called BestMedGrape, the main objectives of which being to support the development of nanotechnological antioxidants/anti-inflammatory/anti-neurodegenerative formulation from grapes through the development of new business opportunities, and to participate in a better preservation of the environment.

Weaknesses and risks linked to the context

No major weaknesses have been identified.

RECOMMENDATIONS TO THE TEAM

The PIs of the team may apply to ERC grants.

Team 7: PERINATAL IMPRINTINGS AND NEURODEVELOPMENTAL DISORDERS

Name of the supervisor: Françoise Muscatelli

THEMES OF THE TEAM

Team 7 addresses fundamental mechanisms of neuronal circuits development by investigating the role of factors that translate the early life environment into lasting physiological and behavioural responses, to better characterise, diagnose and treat neurodevelopmental disorders. The team focuses mainly on oxytocin, leptin and the control of chloride homeostasis as critical players connected to the environment, which control the maturation of neurons and neural networks. For this purpose, the team investigates the abnormalities observed in pre-clinical models of neurodevelopmental diseases at the molecular, neuronal, network, physiological and behavioural levels.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The recommendations made in the previous evaluation were targeted to the two previous teams which merged to build the current team. Because of this profound restructuring of the team and its projects, these recommendations became obsolete.

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	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)	3
Subtotal permanent personnel in active employment	10
Non-permanent teacher researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	0
Post-docs	0
PhD Students	9
Subtotal non-permanent personnel	9
Total	10

EVALUATION

Overall assessment of the team

Team 7 develops excellent projects using approaches ranging from the cellular and molecular levels to behaviour to investigate neurodevelopmental diseases. The attractiveness of the team is attested by the recruitment of a young researcher who obtained an ANR JCJC. The scientific production of the team is very good to excellent, and its training activity is excellent. The translational activities of the team are excellent, with the clinical trials using oxytocin as a treatment for Prader-Willi babies.

Strengths and Possibilities linked to the context

The current composition of Team 7 'Early life imprinting and neurodevelopmental disorders' is the result of the fusion, which occurred in 2018 following the INSERM evaluation, of two previously existing teams of INMED, the teams 'Plasticity of GABAergic synapses in health and diseases' and 'Neurodevelopment and genomic imprinting: Prader-Willi syndrome, from genes to therapy'. Team 7 also benefited from the recruitment of a young INSERM researcher in 2017, which obtained a JCJC ANR in 2021, demonstrating its attractiveness to talented young researchers. These reorganisations, taking advantage of the technical and experimental complementarities of the members of the former teams, allowed the development of research projects involving a broad spectrum of expertise from the cellular and molecular to the electrophysiological and behavioural levels. During the last contract term, the team published important original sets of data, demonstrating that chloride homeostasis, controlling the inhibitory strength of GABA, is impacted in neurodevelopmental diseases with autistic spectrum disorder, and unravelling the impact of hormonal imprinting on brain development and functioning in neurodevelopmental diseases. Along this latter line of research, the team notably showed that oxytocin administration in neonates shapes hippocampal circuitry and restores social behaviour of a pre-clinical model of autism, and that the oxytocinergic system regulates central cardiorespiratory coupling (ANR JCJC OT-CardioResp project). The scientific production of Team 7 is very good to excellent, as demonstrated by a total of six reviews (including one in *Cur Opin Neurobiol*) and 25 original papers issued without collaboration with other teams of INMED. Seven of them were signed as first, last or corresponding author by team members in renowned journals like *Mol. Psy.*, *eLife* (2 papers) and *Mol. Brain*. Team 7 members also co-authored eleven additional papers in collaboration with other INMED teams, demonstrating the high level of collaboration between Team 7 and the other teams of INMED. The research of the team is supported by international (NIH) and national (2 ANR and 1 PIA Centuri project) public funds, as well as by Foundations (NARSAD, Prader-Willi, Lejeune, FRC, Fritz Thyssen Stiftung) and private Companies (Tonix Pharmaceuticals, Astra Zeneca, Axonis Therapeutics). The team develops outstanding translational activities, in close collaboration with clinicians, based on the results they obtained in pre-clinical models of neurodevelopmental diseases. Importantly, the pre-clinical results showing that peripheral oxytocin administration in the first week of life restores normal feeding behaviour in neonates and social behaviour and cognition up to adulthood in a pre-clinical model of rare disease (world patent delivered in 2015, European delivered in 2016, licensing to three companies, one of them sponsoring the team's research) lead to clinical trials now in phase 3 in Prader-Willi babies.

Weaknesses and risks linked to the context

The sharing of knowledge with the public is limited.

RECOMMENDATIONS TO THE TEAM

The sharing of knowledge with the public may be enhanced, especially given the translational character of the research conducted in the team, which would merit higher visibility in the society.

The team is encouraged to apply for additional funds, especially to international calls based on its rich network of international collaborations, to allow the recruitment of postdoctoral fellows. The team is also encouraged to more actively participate in scientific conferences.

The committee recommends working on preparing the future of the team during the coming contract and encourages the team to bring young researchers to the forefront.

Team 8: THE SENSORIMOTOR LEARNING LAB

Name of the supervisor: David ROBBE

THEMES OF THE TEAM

The research of team 8 addresses the contribution of the dorsal striatum (DS) and its cortical inputs to adaptive decision-making and motor control. The team uses original and refined behavioural procedures, state-of-the-art techniques for the recording and manipulation of neuronal activity, and applied mathematical modelling, to elucidate the type of data computed and encoded by the DS during decision-making and motor control. Complementary research axis explored the DS from its inner neurophysiology and control by cortical inputs to its functional role in decision-making.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

To establish more international relationships to enhance the profile, in particular to recruit postdocs who will bring expertise.

The team acknowledges that it could develop more international collaborations. Still, it recruited five and supervised nine postdocs, and their significant contribution is testified by papers' authorship.

Expectation of outreach should be conservative to prevent distraction from research success.

The team has maintained a significant outreach activity, and it did not compromise success in research activity apparently.

Technology developments made would be useful for the broader scientific community, but this has not been exploited.

The previous committee appears to refer to the team's expertise in behaviour and mechatronics. There seems to be a plan for the development of a platform with dedicated staff. How the team will contribute to and benefit from this platform will be questioned.

Better technical support is required, and this group should be supported to recruit an engineer and a PhD student.

The team managed to finance six non-permanent technical staff but has no permanent support staff yet. The second recommendation must concern a PhD student involved in technical developments. It was taken into account with a student from the CENTURI PhD program.

Sort out a more practical solution for chronic animal work. The team has found a way to adapt to the constraints.

WORKFORCE OF THE TEAM

Permanent personnel in active employment	
Professors and associate professors	0
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	2
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	0
Subtotal permanent personnel in active employment	3
Non-permanent teacher researchers, researchers and associates	0
Non-permanent research supporting personnel (PAR)	0
Post-docs	2
PhD Students	3
Subtotal non-permanent personnel	5
Total	8

EVALUATION

Overall assessment of the team

The team stands out for very original research and outstanding integration of the researchers who joined the leader in 2018 and 2020. Visibility, funding, and production are excellent. Five postdocs were recruited, five PhD students supervised, one researcher became a member of a CNRS section. Four ANR contracts were obtained as PI. Publications include nine papers, six as PI in excellent journals (PNAS, 2 Current Biol) and three as partners in excellent to outstanding journals (Nature Comm, Elife), plus a review and a book chapter. Outreach activity is outstanding with original activities such as a theatre play.

Strengths and Possibilities linked to the context

Scientifically, the team applies an outstanding approach. It develops *ad hoc* original behavioural models and mathematical modelling of behaviour together with state-of-the-art neurobiological techniques for a refined questioning of the role of the DS. Using this approach, the team made major contributions and broke dogmas. The team is visible and attractive. A CNRS researcher joined the team in late 2020. Her expertise and complementarity to the team at technical and topic levels, her ability to publish in high-profile journals (Nature Comm 2018) are strong benefits to the team. The team leader was promoted DR2 and became a member of a CNRS section in 2021. The team organised three events of international scope (e.g. GDR meeting, a symposium at NeuroFrance). A chapter was produced for a book that gathers contributions from famous names (e.g. S. Dehaene, W. Schultz). Considering the complementarity and quality of their past activity, the association of these three permanent researchers is a guarantee for cutting-edge research. The scientific policy used to integrate into the team's project the two researchers who joined in 2018 and 2020 is outstanding and already attested by joined grants and publications. The team was involved in PhD training. One researcher was part of the executive board of the EUR Neuroschool. Two of the three researchers have defended their HDR. The team supervised five PhD students. Three of them defended after a means PhD duration of 3.3 years and publications as the first author. One of them was awarded a PhD thesis price by the French Society of Neuroscience. PhDs were able to find positions in renowned academic places (e.g. Imperial College London) or as an industry engineer (Scalian). The team is very competitive in national fundraising with four ANRs obtained as PI (between 2017 and 2021) and the success is shared amongst the three researchers. One ANR is a collaboration between the team leader and one of the researchers. The team had an excellent scientific production both quantitatively and qualitatively (past production of the new researcher not included) with nine original articles, one review and one book chapter, i.e. 5.5 publications per researcher over the period, in excellent to outstanding journals (e.g. 2 Current Biology, PNAS as PI; Nature Comm, Elife as partner). The team has four local collaborations, including three at INMED, and one at the IRPHE, nine national and five international collaborations with very renowned scientists (e.g. Lyon; Barcelona; Genova; Pittsburgh) including with clinical researchers (Berlin). Regarding links to society, researchers are equally engaged in numerous and original activities, including a theatre play with national reach, an artistic show on the perception of music and movement, one lay public conference, three workshop classes in high schools, recurrent contributions to 'La Semaine du Cerveau' and Pint of Science. A researcher animates a section of the INMED website.

Weaknesses and risks linked to the context

Although of great quality, collaborations have not yet resulted in international grant applications.

The team implements complex behavioural protocols and equally complex neurobiological techniques. A permanent technical staff could be an asset to support this demanding activity.

RECOMMENDATIONS TO THE TEAM

Continue to develop this original research line and to take the risk of implementing complex and meaningful behavioural models to eventually couple them with advanced neurobiological techniques and apply mathematical modelling.

Creating or integrating international consortia could set opportunities for European or international grant joint applications.

Team 9: DEVELOPMENTAL EPILEPSIES

Name of the supervisor: Pierre SZEPETOWSKI

THEMES OF THE TEAM

The Team has been focused in deciphering the pathophysiological mechanisms associated with three different developmental epilepsies of genetic origin (KCNQ2, Stxbp1, Grin2A). Moreover, the team has started a fruitful investigation related to the non-genetic encephalopathy caused by cytomegalovirus congenital infection. For these studies, the team has implemented a multidisciplinary approach on established or pre-clinical models investigated at pharmacological, neuroanatomical, and electrophysiological levels.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

N/A

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)	1
Post-docs	0
PhD Students	3
Subtotal non-permanent personnel	5
Total	9

EVALUATION

Overall assessment of the team

The Team has developed a consistent research program on three genetic neurodevelopmental disorders (mTor-related brain disorders, Grin2a-related developmental epilepsies and epileptic encephalopathies caused by Kv7.2 or Stxbp1 mutations) and congenital brain CMV infections. The Team has a very good international reputation given its efforts in developing its own and original pre-clinical models for some of these disorders and to use them for the identification of the underlying pathophysiological mechanisms. The scientific production is very good with nineteen original research studies, twelve of which as corresponding authors, published in highly respected scientific journals, but with a rather specialised audience. Doctoral students and technical staff have been successfully integrated in the scientific activities. The Team has not enrolled postdoctoral fellows nor recruited new tenured researchers during the contract period.

Strengths and Possibilities linked to the context

The scientific production is well distributed between the tenured scientists suggesting a balanced scientific output between the scientific personnel. Full-term engineers have also been deeply involved in scientific production and consequently shared the co-authorship in several research articles. The research topics are coherent with the interests and previous achievements of the team and have led to interesting novel mechanistic insights on the pathophysiological basis of the genetic and viral-induced neurodevelopmental epileptic diseases.

Weaknesses and risks linked to the context

The Team has not been able to recruit new tenured researchers for promoting the generational turnover of the scientific personnel. Moreover, the Team has not recruited postdoctoral fellows over the current contract period. The collaborative papers between the different groups within the Team are relatively few suggesting suboptimal interactions for common scientific goals. The team has experienced some difficulties to attract sufficient academic funding which have challenged the full exploitation of research projects.

RECOMMENDATIONS TO THE TEAM

The team as it is now will not be continued for the next coming contract due to the imminent retirements of the three main tenured directors of research of the Team. The Team has not been able to enrol new tenured researchers to follow up these studies within the same team organisation.

Researchers and technicians of this group will integrate Teams 1 and 4 for the next contract period. This change seems to be well thought and coherent with the scientific interests of this group to further pursue its research interests in an excellent environment and to synergistically contribute to Teams 1 and 4 activities. For instance, this new merge will provide the means to extend the investigations on CMV-induced developmental encephalopathy in the framework of Team 1 and the committee recommends the researchers who will integrate that team to apply to competitive calls to pursue independently this original line of research.

CONDUCT OF THE INTERVIEWS

Date(s)

Start: 13 décembre 2022 à 8 h 30

End : 14 décembre 2022 à 16 h

Interview conducted: on-site

INTERVIEW SCHEDULE

December 12th, 2022

Arrival of the committee and evening dinner (only committee members and Hcéres Scientific advisor)

December 13th, 2022

8:30 a.m.-8:45 a.m.	Closed session with the committee
8:45 a.m.-9 a.m.	Presentation of the committee to the unit
9 a.m.-10:00	Presentation of the unit by the present director Ms Rosa COSSART (Plenary session, 40 ' presentation + 20 ' discussion with the committee)
10:00-10:30	Presentation of Team 1: MOLECULAR BASIS AND PHYSIOPATHOLOGY OF CORTICAL DEVELOPMENT DISORDERS (Carlos CARDOSO). (15 ' presentation + 10 ' questions + 5 ' in private PI-committee)
10:30-10:50	Coffee break
10:50-11:20	Presentation of Team 2: DEVELOPMENT OF HIPPOCAMPAL COGNITIVE MAPS (Rosa COSSART). (15 ' presentation + 10 ' questions + 5 ' in private PI-committee)
11:20-1 p.m.	Debriefing of the Visiting committee (closed-door)
1 p.m.-2 p.m.	Lunch with the lab
2 p.m.-2:30 p.m.	Presentation of Team 3: NEUROCODAL CODING AND PLASTICITY IN EPILEPSY (Valérie CREPEL). (15 ' presentation + 10 ' questions + 5 ' in private PI-committee)
2:30 p.m.-3 p.m.	Presentation of Team 4: NEURONAL CODING OF SPACE AND MEMORY (Jérôme EPSZTEIN). (15 ' presentation + 10 ' questions + 5 ' in private PI-committee)
3 p.m.-3:30 p.m.	Presentation of Team 5: EARLY ACTIVITY IN THE DEVELOPING BRAIN (Roustem KHAZIPOV). (15 ' presentation + 10 ' questions + 5 ' in private PI-committee)
3:30 p.m.-3:50 p.m.	Coffee break
3:50 p.m.-4:20 p.m.	Presentation of Team 6: ADOLESCENCE AND DEVELOPMENTAL VULNERABILITY TO NEUROPSYCHIATRIC DISEASES (Olivier MANZONI). (15 presentation + 10 ' questions + 5 ' in private PI-committee)
4:20 p.m.-4:50 p.m.	Presentation of Team 7: PERINATAL IMPRINTINGS AND NEURODEVELOPMENTAL DISORDERS (Françoise Muscatelli). (15 ' presentation + 10 ' questions + 5 ' in private PI-committee)
4:50 p.m.-7 p.m.	Private meeting of the visiting committee (report preparation)
8 p.m.	Dinner in town for the committee

December 14th, 2022

9:00-9:30	<i>Presentation of Team 8: NEURAL BASES OF SENSORIMOTOR LEARNING (David ROBBE). (15' presentation + 10' questions + 5' in private PI-committee)</i>
9:30-10:00	<i>Presentation of Team 9: DEVELOPMENTAL EPILEPSIES (Pierre SZEPETOWSKI). (15 presentation + 10' questions + 5' in private PI-committee)</i>
10:00-10:20	<i>Coffee break</i>
10:20-10:50	<i>Discussion with the representatives of the funding bodies</i>
11:00-11:30	<i>Meeting with team leaders, without the lab director</i>
11:30-1 p.m.	<i>Private meeting of the visiting committee (report preparation)</i>
1 p.m.-2 p.m.	<i>Lunch (committee only)</i>
2 p.m.-2:30 p.m.	<i>Meeting with engineers, technicians and administrative personnel (in French)</i>
2:30 p.m.-3 p.m.	<i>Meeting with students and postdocs</i>
3 p.m.-3:30 p.m.	<i>Meeting with scientists, without the team leaders and lab director</i>
3:30 p.m.-4 p.m.	<i>Discussion with the director, Rosa COSSART</i>
4 p.m.	<i>End of the visit</i>

PARTICULAR POINT TO BE MENTIONED

- The INMED platform 'Tous Chercheurs' is a very original and successful structure for the diffusion of scientific education and arousing new vocations for scientific careers amongst the young public, and thereby fully meets the expectations of the INMED institutions in the field. The committee strongly supports the activities of this platform and thus recommends Inserm and Aix-Marseille University to provide the modest but nevertheless essential support for the continuation of its activities that are unique in France.
- The committee points out the importance of hiring tenured engineers on the INMED platforms (e.g. the behavioural testing platform) that still lack such permanent positions, which are essential for the full exploitation of their technological potential by the INMED staff, especially PhD students and postdocs.
- The committee also points out the urgent need to increase the number of formations to surgery available for newly recruited PhD students or postdocs, that are mandatory for conducting most if not all INMED projects.
- Finally, the committee wishes to stress the importance of rapidly implementing a remote backup of the INMED data in another building. The INMED management team is aware of the risks and the committee recommends the INMED institutions to assist the unit in rapidly solving this issue.

Réunion avec les ITAs de l'INMED.

Pendant l'évaluation, nous avons visité une partie des locaux de plusieurs équipes, de la plate-forme INMAGIC et de l'association «Tous Chercheurs» au sein de l'Inmed.

Nous voulons particulièrement souligner les actions originales de «Tous Chercheurs» dans les domaines de vulgarisation et de la promotion des métiers de la recherche. Cette structure d'intérêt collectif mériterait largement d'être récompensée par un soutien supplémentaire de l'INSERM et de l'université Aix Marseille.

Ces visites très enrichissantes par leurs échanges se sont conclues par une réunion avec l'ensemble des ITA, ITRF et des élus. Grâce à la qualité des échanges lors de cette réunion et l'investissement des participants, sont ressorties des pistes d'amélioration.

Ainsi, nous faisons quelques remarques et propositions concernant l'organisation et la vie des ITA au sein de l'Inmed.

- 1) Bien que des ITA soient bien élus et siègent au conseil d'unité il semble que l'information ne soit pas connue de l'ensemble du personnel. Une organisation en comité ITA avec des réunions mensuelles pourrait améliorer la diffusion de l'information et permettre des échanges plus constructifs entre la direction et les ITA.

- 2) Le mode de classement des dossiers GAIA au niveau de l'unité ne semble pas acquis pour tous les agents ITA. La mise en place de rapporteurs afin de mieux évaluer les dossiers, accompagnés d'observateurs ITA permettrait de rendre ce classement plus compréhensible
- 3) Enfin nous proposons la création d'une charte d'éthique pour une meilleure reconnaissance des travaux effectués par les ITA car le chiffre de 55 % des articles de recherche avec au moins un ITA de l' Inmed paraît faible.

GENERAL OBSERVATIONS OF THE SUPERVISORS

Le Président de l'université

au

Département d'Évaluation de la recherche -
Hcéres

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

N/Réf. : VPR/LS/AMS/CM – 23-07

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Vos réf :

DER-PUR230023170 - INMED - Institut de neurobiologie de la Méditerranée

Marseille, le jeudi 15 juin 2023

Madame, Monsieur,

Je fais suite au mail que vous nous avez adressé le 30/05/2023 dans lequel vous me communiquiez le rapport d'évaluation Hcéres de l'Unité INMED - Institut de neurobiologie de la Méditerranée.

Comme demandé dans ledit mail, je vous fais part des observations de portée générale en reportant les commentaires de l'unité:

Réunion avec les ITA de l'INMED.

Pendant l'évaluation, nous avons visité une partie des locaux de plusieurs équipes, de la plate-forme INMAGIC et de l'association « Tous Chercheurs » au sein de l'Inmed.

Nous voulons particulièrement souligner les actions originales de « Tous Chercheurs » dans les domaines de vulgarisation et de la promotion des métiers de la recherche. Cette structure d'intérêt collectif mériterait largement d'être récompensée par un soutien supplémentaire de l'INSERM et de l'université Aix Marseille.

Ces visites très enrichissantes par leurs échanges se sont conclues par une réunion avec l'ensemble des ITA, ITRF et des élus. Grâce à la qualité des échanges lors de cette réunion et l'investissement des participants, sont ressorties des pistes d'amélioration.

Ainsi, nous faisons quelques remarques et propositions concernant l'organisation et la vie des ITA au sein de l'Inmed.

- 1) Bien que des ITA soient bien élus et siègent au conseil d'unité il semble que l'information ne soit pas connue de l'ensemble du personnel. Une organisation en comité ITA avec des réunions mensuelles pourrait améliorer la diffusion de l'information et permettre des échanges plus constructifs entre la direction et les ITA.

Nous souhaitons apporter un rectificatif à cette mention ; ce rectificatif a été rédigé et validé par tous les ITA de l'unité :

« La liste du personnel élu et nommé au conseil de centre est disponible auprès de l'administration et est communiquée à tout le personnel du centre. La composition du Conseil de Centre est annexée au règlement intérieur transmis à chaque nouvel entrant et disponible sur l'Intranet.

Nos représentants ITA transfèrent les ordres du jour et les dates des différents conseils du centre à tous les ITA (statutaires ou contractuels). Depuis mai 2023, les ITA ont parmi leurs représentants au conseil de centre un ITA non statutaire.

Depuis l'année dernière et la mise en place d'un « comité ITA » en juin 2022, à l'initiative des ITA eux-mêmes, il est convenu que 2 fois par an, les ITA organisent des demi-journées d'échanges et de dialogues afin de centraliser les besoins remontés à la direction. Ainsi nous souhaitons améliorer la diffusion de l'information au sein des différents services et équipes.

- 2) Le mode de classement des dossiers GAIA au niveau de l'unité ne semble pas acquis pour tous les agents ITA. La mise en place de rapporteurs afin de mieux évaluer les dossiers, accompagnés d'observateurs ITA permettrait de rendre ce classement plus compréhensible

Idem, nous souhaitons apporter un rectificatif à cette mention; ce rectificatif a été rédigé et validé par tous les ITA de l'unité :

Depuis le début du mandat (2018), la direction actuelle a instauré une discussion collégiale au sein du comité de direction (les chefs des différentes équipes) des classements des dossiers GAIA de l'Inmed. Ce classement est associé à une réflexion avec le Responsable des Ressources Humaines PACA. L'idée est de promouvoir le maximum de dossiers.

Lors de la réunion des ITA de février 2023, invité par ces derniers comme suite à la visite HCERES de décembre, le RRH PACA est intervenu pour expliquer toutes les voies possibles de promotion et rappeler l'importance des sélections professionnelles et des concours internes. L'Inmed peut notamment se féliciter cette année du nombre de dossiers éligibles déposés aux concours internes et sélection professionnelle (7 sur 21, soit 33% des ITA statutaires susceptibles d'être admis à concourir).

- 3) Enfin nous proposons la création d'une charte d'éthique pour une meilleure reconnaissance des travaux effectués par les ITA car le chiffre de 55 % des articles de recherche avec au moins un ITA de l'Inmed paraît faible.

Idem, nous souhaitons apporter un rectificatif à cette mention ; ce rectificatif a été rédigé et validé par tous les ITA de l'unité :

En Conseil de Centre et en Comité de Direction, en décembre 2021, une mention spécifique en ce sens a été rédigée puis validée et diffusée à tous les personnels ; le règlement intérieur a été mis à jour.

Vous souhaitant bonne réception des présentes,

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

Eric BERTON



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

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