Research evaluation

EVALUATION REPORT OF THE UNIT

3PHM – Physiopathologie et Pharmacotoxicologie Placentaire Humaine, Microbiote pré & post natal

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Université Paris Cité,
Institut national de la santé et de la recherche médicale – Inserm

EVALUATION CAMPAIGN 2023-2024
GROUP D

Rapport publié le 04/03/2024

High Council for evaluation of research and hgher education

In the name of the expert committee[1] :

Nicole, Hagen, Chairwoman of the committee

For the Hcéres[2] :

Stéphane Le Bouler, acting president

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

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

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

MEMBERS OF THE EXPERT COMMITTEE

Chairperson:	Ms Nicole Hagen, École Nationale Vétérinaire de Toulouse
Experts:	Ms Christiane Forestier, Université Clermont Auvergne, Clermont Ferrand (representative of CNU) Mr Laurent Galio, INRAE, Jouy-en-Josas (supporting personnel) Ms Hafida Khorsi-Cauet, Université de Picardie Jules Verne Ms Aminata Touré, CNRS, La Tronche (representative of Inserm)

HCÉRES REPRESENTATIVE

Ms Muriel Mercier-Bonin

REPRESENTATIVES OF SUPERVISING INSTITUTIONS AND BODIES

Xavier Descleves - Pharmacy Department - Faculty of Health - Université Paris Cité
Christine Guillard - Faculty of Health - Université Paris Cité
Claire de Marguerye - Inserm Delegation - Paris Île-de-France Centre Nord
Matthieu Resche-Rigon - Dean of the Faculty of Health – Université Paris Cité
Jean Rosembaum, Inserm theme-based institute Cell biology, Development and Evolution

CHARACTERISATION OF THE UNIT

- Name: Pathophysiology & Pharmacotoxicology of the Human Placenta, pre & postnatal Microbiota
- Acronym: 3PHM
- Label and number: UMR-S1139
- Composition of the executive team: Mr Thierry Fournier (director) and Mr Frédéric Barbut (deputy director)

SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement
SVE6 Physiologie et physiopathologie humaine, vieillissement

THEMES OF THE UNIT

The 3PHM unit is structured in two research groups (placentologist group and microbiologist group) led respectively by the unit director and the deputy director, and corresponding to the two scientific axes, ontogeny of the placenta in normal and pathological conditions and newborn intestinal microbiota. These two biological systems are key determinants of the foetal and neonate development during the first 1000 days, a period decisive for the lifelong health.
The first axis focused on the development and function of the chorionic villi both in normal and pathological pregnancies and the relationship with foetal growth restriction. Several molecular and pathways were investigated in normal and pathological conditions (anoxia, chemical contaminants and pathogens): (1) the redox and metabolic status of the trophoblast and its adaptation to oxidative stress; (2) the nuclear receptor PPARγ and its role in placental development; (3) the role of the detoxification receptor, aromatic hydrocarbon receptor and (4) the implication of interferon in placental dysfunction. The effects of several environmental pollutants, such as phthalates, polycyclic aromatic hydrocarbons (PAHs), nanoparticles or nano/microplastics on the placental function were evaluated.
The issue of placental development and health is addressed along a continuum between fundamental and translational research. The latter involves (1) the identification of maternal biomarkers of the implantation and pregnancy outcome, such as human Chorionic Gonadotropin (hCG) glycoforms signature, and (2) the development of new therapeutic approaches (apheresis, nanomedicine) to treat pregnancy-related diseases without side effects for the foetus.
The microbiota research program includes two thematic axes: (1) the microbiome establishment in the neonate, targeting premature infants and its consequences on the child's health and (2) the development of preventive and therapeutic approaches of gut microbiota dysbiosis. The first thematic axis associates a global approach to the microbiome, as well as a more targeted approach. The former includes: (1) the evaluation of the possible contribution of placental microbiota on the gut colonisation, integrating the two groups of research; (2) the influence of prematurity and of practices of neonatal intensive care on the impaired bacterial colonisation. The latter focused on (1) the dynamic of colonisation of *Clostridioides difficile* and *Bifidobacterium* in preterm neonates and (2) the pathophysiological role of *Clostridium butyricum* and *C. neonatale* in the occurrence of the necrotising enterocolitis in preterm infants.
This microbiota program includes both basic and translational research, aiming to manipulate therapeutically the neonate microbiota by using probiotics and faecal microbiota transplantation, in order to prevent and cure dysbiosis and associated diseases, such as necrotising enterocolitis, allergies and irritable bowel syndrome.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The UMR-S 1139 'Pathophysiology & Pharmacotoxicology of the Human Placenta; pre & postnatal Microbiota' (3PHM) was created in 2018, with a DR Inserm as director and a PU-PH as deputy director. It results from the merger of two units: UMR-S1139 'Pathophysiology & Pharmacotoxicology of the Human Placenta' created in January 2014 and EA 4065 'Intestinal ecosystem, probiotics, antibiotics' created in 2006, renewed in 2010, and again in 2014. These units are included in the department 'Biology & Health of mother & child' founded in 2009 in the Faculty of Pharmacy Paris Descartes, which took an active part in the founding of the Hospital-University-Department 'Risks in pregnancy'.
The unit is located at the Faculty of Pharmacy of Paris, the same location of the two previous research units. Nevertheless, the two groups, focused respectively on the placenta and neonate intestinal microbiota, are located in two different levels of the Faculty of Pharmacy.

RESEARCH ENVIRONMENT OF THE UNIT

The unit is administered by both Inserm and Université Paris Cité.
As a member of the IP2S ('Institut Pharmacie Sciences et Santé'), 3PHM benefits from all technical platforms of University Paris Cité (animal facilities, imaging platform, flow cytometry, real-time PCR equipment), in particular at the Faculty of Pharmacy. They also benefit of Institut Cochin platforms (GENOM'IC, HistIM, Protéomique 3P5 etc.).
3PHM belongs to two Doctoral Schools: ED 562-BioSPC (Bio Sorbonne Paris Cité) and ED 563-MTCI (Drug, Toxicology, Chemistry, Imaging). ED 562-BioSPC is divided into 4 departments. 3PHM belongs to three of them:

Cellular and Molecular Biology, Physiology, Physiopathology (BCMPP); Development, Genetics, Neurobiology, Reproduction and Aging (DGNRV) and Infectiology and Microbiology (IM).
3PHM members are founders/members of numerous institutions and research groups on pregnancy, perinatality and microbiota both at the national level (French Group of Faecal Transplantation (GFTF), Technical Committee of Vaccination (CTV), CES (Committee of Scientific Experts) of the GIRCI ('Groupement Interrégional pour la Recherche Clinique et l'Innovation') of Ile de France) and at the international level (treasurer of the ESGCD (European study group on *Clostridioides difficile*), co-organiser of the International *C. difficile* symposium (ICDS), French coordinator of COMBACTE-CDI (Combacting bacterial resistance in Europe – *C. difficile* infection), member of EuroToxemia and co-organiser of the meeting and member of European Placental Group, 'Groupe de la francophonie Placentaire' (GfP)).
3PHM has founded PremUp, a foundation to win the battle against prematurity. It participates to the Labex Institut Pierre Gilles de Gennes and to the Idex prematuration (MERIT) 2021, created as a part of the PIA (future investment program).
3PHM is involved in regional or national networks. It is affiliated to the Hospital- University-Department (DHU) 'Risks in pregnancy'. 3PHM created and has directed the FHU ('Fédération Hospitalo-Universitaire') PREMA, 2020. It is also member of the FHU PaCeMM 'Paris Center for Microbiome Medicine', the FHU SENEC and the COPIL 'Institut Hors-Murs Santé des Femmes', Université Paris Cité. It actively participates to the 'Institut de Microbiologie Hors-Murs', Université Paris Cité. It has developed and is responsible for the germ-free animals in the platform 'Anima'. It directed the national reference centre (CNR) *Clostridioides difficile*.
3PHM is involved in international networks. It is implicated in a European Paediatric Translational Research Infrastructure program (EPTR, Horizon 2020), partnership with Université Paris Cité. In this context, 3PHM is a member of Placentech®, a placental platform.
3PHM participates to the constitution of several cohorts of newborns (ELFE, EPIFLORE, ClosNEC, etc.), the Apheresis cohort, the COVIPREG cohort (COVID & Pregnancy). It also participates to the multicentre randomised trial (RANSPRE).

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

Catégories de personnel	Effectifs
Professeurs et assimilés	8
Maîtres de conférences et assimilés	11
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	14
Sous-total personnels permanents en activité	**34**
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	9
Sous-total personnels non permanents en activité	**9**
Total personnels	**43**

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

Nom de l'employeur	EC	C	PAR
UNIVERSITÉ PARIS-CITÉ	19	0	10
Inserm	0	1	3
AUTRES	1	0	3
Total personnels	**20**	**1**	**16**

GLOBAL ASSESSMENT

Unit description

The UMR-S 1139 research single-team unit, entitled 'Pathophysiology & Pharmacotoxicology of the Human Placenta; pre & postnatal Microbiota' (3PHM) is structured in two research axes related to the impact of the materno-foetal environment (gut microbiota, pollutants, metabolism, genetic variants, etc.) on the development and functions of the placenta, the reproductive function and on the health of the newborn and the child. This research is focused on the first 1000-day period, decisive for the health of the future adult.

3PHM is headed by its current director and its deputy director since 2018, corresponding to the merger of two units, UMR-S1139 'Pathophysiology & Pharmacotoxicology of the Human Placenta' and EA 4065 'Intestinal ecosystem, probiotics, antibiotics'. 3PHM is affiliated with both Université Paris Cité (Faculty of Pharmacy of Paris) and Inserm. It currently hosts about 34 permanent staff members (25 from Université Paris Cité, 5 from Inserm, 4 others).

The unique combination of expertise and approaches (*in vitro* and animal models, organoids, cohorts…) and the close interactions between researchers, clinicians and teachers grouped together in the same team allow a continuum between cognitive and translational research necessary for the development of diagnosis and therapeutic innovations. The unit is well connected within a local and regional network of diverse scientific, clinical, and technological expertise. The strong implication of the members of the unit in FHU ('Fédérations Hospitalo-Universitaires', FHU PREMA (fighting prematurity), FHU for Microbiome Medicine) facilitates the collaboration with clinical departments and allows the constitution of birth cohorts (like RANSPRE, ELFE, EPIPAGE 2…). The unit has further access to technological experimentation support and animal facilities of the Université Paris Cité and of Institut Cochin.

Attractiveness

The attractiveness and international visibility of the 3PHM are overall excellent.

Financial resources are mostly from competitive call applications at the national and European levels and industrial collaborations to reach 61% of total funding (salaries of permanent staff not included).

At the EU level, two BINC grants (Biostime Institute Nutrition & Care) are coordinated by the unit (MicroKid: 50 k€ and Primal: 40 k€ for 3PHM). Eight national contracts out of ten were obtained as PI, including ANR PregNanoBaP (326 k€), ANR PEfingerprint (438 k€, total), ANR ClosNEC (156 k€), PHRC T FORE (329 k€). The unit also benefits from eight contracts funded under the PIA (idex, i-Site, Labex) including 6 as PI, for example: PROFIT (prematuration and Idex, 110 and 85 k€ respectively); FHU PREMA (75 k€), Labex IPGG/premUp (200 k€).

It has also actively participated in various committees at the national level (e.g. FHU PREMA) and, at the European level, COMBACTE-CDI (Combacting bacterial resistance in Europe – *C. difficile* infection) consortium and EuroToxemia and Placental groups, enhancing its integration into the fields of placenta/prematurity and newborn gut microbiota research and its leadership position. The unit maintains a strong scientific reputation, exemplified by about 50 invited conferences and by its involvement in the organisation of five international meetings (for example, Eurotoxemia – Paris 2018, International *Clostridium difficile* symposium, ICDS - 2018 and 2020, European Society for Reproductive Immunology, ESRI – Paris 2022, International Society for the Study of Hypertension in Pregnancy, ISSHP – Montpellier 2022) and one national scientific meeting. The unit has been successful in recruiting 4 young researchers/teachers/hospital practitioners for permanent positions within Inserm and the university, contributing to its dynamism. Furthermore, eight PhDs were defended for eleven HDR holders in the Unit.

To maintain its leadership position and financial resources, the unit should apply to European and national competitive calls and for example to calls from the PEPR project led by Inserm 'Santé des femmes et des couples'. Solving infrastructure problems, such as the premises of the microbiota group at the Faculty of Pharmacy of Université Paris Cité, could enhance the unit's appeal. The unit could improve its efficiency by securing support staff responsible for managing administrative, financial, and logistical responsibilities. This would streamline internal processes and free up resources for research itself.

Scientific production

The unit has significantly contributed to increasing the knowledge on the pathophysiology of placental development and the microbiome establishment in the neonate and the consequences on the newborn and child health. The microbiologist group succeeded in isolating many interesting strains: (i) strains able to prevent colonisation by pathogenic *C difficile* in an animal model (patent deposited in 2020 with an application for European extension from 2021); (ii) three strains of Bifidobacteria able to protect from neonatal necrotising enterocolitis lesions; (iii) three other probiotic strains (*Lactobacillus* and *Bifidobacterium*) able to exert preventive effects in a mouse model of cow's milk allergy; (iv) strains of *Bifidobacterium* able to improve *in vitro* and *in vivo* the dysfunctions associated with irritable bowel syndrome.

The unit has established a highly productive research program yielding an excellent scientific production. Over the past five years, the unit's members have published a total of 201 original papers and twenty reviews in high-profile generalist (Science, Nature Medicine and Nature Communications) or speciality journals (e.g. Gut Microbes, American Journal of Clinical Nutrition, American Journal of Pathology, American Journal of Transplantation, Allergy, Hypertension, Environmental Health Perspectives, Journal of Cellular and Molecular

Medicine), mostly as first and/or last/co-last authors emphasising the visibility of their research. The unit's scientific output is impressive, averaging 2.2 original papers per scientist per year, for a total of only one full researcher and fourteen researchers/teachers of whom several are hospital practitioners.
The unit encourages the participation of both senior and junior PIs in publications, fostering collaboration and increasing research productivity.
Despite the challenges posed by the COVID-19 pandemic, the unit has actively participated in international and national scientific meetings through oral presentations and posters, enhancing its international visibility.
The unit has set up an operative strategy for scientific integrity and open science through efficient traceability of raw data and deposit in public databases together with reviewing of all experimental protocols by trained and experienced technical laboratory staff. But there is no formalised FAIR Data management plan strategy and the unit should promote open science by systematically publishing preprints in open-access repositories.
However, there is clearly a division of the two research axes, microbiota and placenta, with an only common publication between the microbiota and placenta groups, even though the unit is keen to develop joint research projects. To foster collaboration and scientific cohesion within and between themes, it is advisable to consider the microbiota of the mother and newborn as a key element in the relationship between materno-foetal environment (including pollutants and maternal metabolism) and child health.

Contribution to Society
The unit has obtained promising results in the development of biomarkers, which could be good candidates for the early diagnosis of gut microbiota dysbiosis or pathological pregnancy (such as interferon for pre-eclampsia) and in the development of therapeutic strategies of gut microbiota dysbiosis (probiotic and faecal microbiota transplantation).
The unit has developed collaborations with economic players as illustrated by the thirteen contracts with industry directed by a member of the unit, for example with PILeJe (probiotics and allergy, 242 k€), IBIS (probiotics and irritable bowel syndrome, 160 k€) and COVID Fast Track (172 k€ total), CONTRABUG (Maat Pharma, 155 k€) and SANOSAFE (Sanofi Pasteur, 315 k€ total) and expertise activities (Besins, Bledina, Havea and Tillots, Pfizer, MSD, Astellas). It has also developed partnerships with foundations or charities (e.g. 'Fondation de France', 'Fondation Roveltain', 'Un sourire pour Hirschprung').
In addition, the unit actively participates in public outreach endeavours (publication of 9 book chapters, 25 articles in newspapers and magazines, webinars, and interviews) and in science promotion operations targeting health professionals, high school students (DECLICS program) and general public (for example, organisation of the symposium dedicated to women's health and the coordination of the Women's Health Institute project fully in line with the Ile de France site policy (Université Paris Cité).
However, despite their significant contribution to translational research, the unit has not been actively involved in commercial exploitation of their findings (2 patent-pending on probiotics to prevent necrotising enterocolitis and on a procedure of faecal microbiota transplantation preservation). This activity should be expanded to provide additional resources to the lab through increased interaction with SATT and Inserm-Transfert for example.
It is surprising to note that members of 3PHM have not been actively involved in Health authorities' committees (e.g. ANSES, 'Haute Autorité de Santé' (HAS).

DETAILED EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Responses to the three recommendations of the previous HCERES report on 3PHM are not explicitly addressed but some information incorporated in the self-evaluation document and completed during the interview show that progress has been made in particular to encourage exchanges and the construction of projects between the two groups, placenta and microbiota, despite their separate geographical locations.

Recommendations on scientific production and activities

On the reporting period, the scientific papers of the 3PHM unit were published in very good or excellent disciplinary journals (for example, Gut Microbes, American Journal of Clinical Nutrition, American Journal of Pathology, American Journal of Transplantation, Allergy, Hypertension, Environmental Health Perspectives, Journal of Cellular and Molecular Medicine) or in high-impact generalist journals (e.g. Science).

3PHM has extended its international collaborations as shown by the recruitment of international postdoctoral researchers and graduate students and the raising of European funding.

Recommendations on the unit's organisation and life

A MCU in microbiology joined the group microbiota and allows the development of new projects in microbial genetics. A CRCN Inserm, with 100% of his time dedicated to research, will join the group placenta. However, this researcher will develop a new research axis on the effect of minipuberty dysfunction on the female fertility and puberty.

As recommended, exchanges and collaborations between the two groups have been facilitated by the organisation of weekly meetings and a two-day annual retreat to build consensus and engage all staff. The organisation plan of the co-location of the two groups has been built, facilitating the exchanges between the two groups, placenta and microbiota, but this is a medium – to long-term project requiring investments from the supervisory authorities.

Commissioned by the supervisory authorities, an external Science Advisory Board (SAB) performed two audits of research department of the Faculty of Pharmacy, in 2021 and 2023. These audits highlighted the dilapidated state of the premises at the Faculty of Pharmacy of Université Paris Cité and the need to renovate them. They also approved the structuration into four research axes. However, this audit encompassed all the Faculty of Pharmacy's research units, making it difficult to apply this analysis to 3PHM and to position the unit within these axes 3 or 4.

Recommendations on scientific strategy and projects

Several projects have been developed at the interface between the two groups, placenta and microbiota. However, the demonstration that the placenta does not harbour a microbiota limits its contribution to the establishment of the neonate microbiota and further interaction between the two groups. Nevertheless, other collaborative projects are in progress to evaluate the capacity of microbiota to activate the studied placental molecular signalling pathway.

B – EVALUATION AREAS

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

Assessment on the scientific objectives of the unit

The scientific objectives of 3PHM focused on the so-called 1000-day period concept and integrating basic and translational research are excellent. Shared research projects integrating maternal microbiota and placental function have been initiated.

Assessment on the unit's resources

The profile, resources and organisation of the unit are excellent, based on the great investment of human resources and despite heavy clinical or teaching duties.

Assessment on the functioning of the unit

The functioning of 3PHM is very good in terms of infrastructure because it benefits from all technical platforms of Université Paris Cité but their premises are in poor conditions and need renovation. The functioning of the unit is excellent in terms of human interactions, collegiality and general organisation. This organisation is based on quality procedures and is facilitated by both the great expertise of the technical staff and the availability of supervisors.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

The two objectives of 3PMH are ambitious and very relevant to both scientific and medical issues in obstetrical diseases and prematurity and their consequences on the lifelong health. Moreover, the investigation on placental function includes the maternal environment, in particular chemical contaminants such as particulate plastics, PAHs or nanoparticles, which have major impact for public health. They address great medical, scientific and societal issues related to the management of the Developmental Origins of Health and Disease (DOHaD) concept.
They are fully in line with the policy of Inserm and are integrated in the research strategy of Université Paris Cité. 3PHM is well placed to fulfil these scientific objectives and even more if it is able to combine the skills of the two groups to carry out innovative projects.

Weaknesses and risks linked to the context

The objectives of the placenta and microbiota groups do not appear to be sufficiently integrated as yet. The investigation of the placental microbiome was a first step. Scientific questions concerning the effects of early alterations of the exposome (pollutants, malnutrition…) on the development and functions of the placenta, the outcome of pregnancy, including reproductive functions and minipuberty, are now integrating the mother's microbiota or the establishment of the newborn's microbiota, but are not yet fully addressed.

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

Strengths and possibilities linked to the context

The thematic organisation of the 3PHM unit reflects their determination to define complementary scientific questions.
The unit benefits from all technical platforms or facilities of Université Paris Cité (molecular and cellular analysis equipment, statistical analysis, imaging platform and animal facilities).
Human resources increased (2 MCU, 1 MCU-PH, 1 IE, 1 AI and 1 administrative support (40%)) in the reporting period, reflecting the attractiveness of the research performed in the unit. New arrivals (1 CR, 1 AI and 1 TR) in the near future will help to compensate for departures (1 PU, 1 MCU-PH and 1 PU-PH), reinforce the technical staff and create a new research axis. The unit has a high proportion of technical laboratory staff with complementary expertise. The strong contribution of teachers-researchers who are also hospital practitioners enables the development of multi-disciplinary and translational research. Furthermore, additional activities of PU-PH and MCU-PH are compensated by collective efforts from technical laboratory staff and MCU. Moreover, strong links with the hospital resource facilitate the constitution of human cohorts with longitudinal clinical follow-up and biological collection.
The unit benefits from a balanced proportion of recurrent funding by Inserm (around 90 k€ per year) and Université Paris Cité (around 43 k€ per year). From 2017 to 2022, the 3PHM unit made significant efforts to get additional funding (regional, national public funding and private funding) in order to increase considerably their resources (137 to 383 k€ per year) facilitating their research activities.

Weaknesses and risks linked to the context

The geographical separation of the two groups of the unit still limits emergence of joint projects and an entire collective life and the possibility to share technical laboratory staff.

The poor conditions of the premises of the microbiota group hinder operators' safety and there is a lack of space for the placenta group's premises. They have participated in the project to regroup geographically the two groups, which was postponed.
There is a high proportion of teacher-researchers with clinical/teaching activity, which limits the time devoted to research and PhD students and/or post-doc supervision.
A strong administrative support is missing, with only one person sharing her time between 3PHM and two other units.

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

Strengths and possibilities linked to the context

The functioning of the unit complies with the regulations on human resources management. The unit has a laboratory council, with elected representatives, which meets at least twice a year. They have scientific intra and inter-axes regular meetings to encourage communication between all members of the different groups. They have a research unit's internal code that every new member, including trainees, must read and sign. This document exposes all the rules and guidelines of the unit, ethical rules and properties rights as well as safety recommendations, including preventive procedures and recommendations concerning accident at work.
The unit is fully aware of the necessity to tend to have a gender equity in their organisation, whenever possible, for the recruitment of postdoctoral researchers, or doctoral or Master 2-degree students.
The promotion of the University and Inserm staff is supported by the managers and all staff members have access to Inserm and Université Paris Cité training.
A special attention is paid by the unit to raw data back-up and efficient traceability. The protocols and process are reviewed by technical laboratory staff whenever necessary. The interoperability of procedures and biological collection is made possible by file sharing and identification of biological samples.
The technical laboratory staff is highly involved in the technical developments required for the research projects and in the training of the students (PhD or Master) and researchers. All the exchanges between ITAs and researchers/teachers-researchers/hospital practitioners relative to the scientific projects contribute to the dynamism of the research and reveal the collegiality within the unit.

Weaknesses and risks linked to the context

Premises are old and not fully suitable for pathogen handling; in this regard, a Level 2 (L2) laboratory is missing.
The molecular biology laboratory has no efficient ventilation system, windowless and timeworn rooms.
The unit does not have a coordinated purchasing management.
In spite of the research unit's internal regulations, procedures regarding safety and psycho-socio risks are poorly known by new arrivals.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The attractiveness of 3PHM is excellent.
The researchers are active members of national and European research groups such as FHU PREMA and COMBACTE-CDI consortium, indicative of their scientific recognition and expertise in their field. The attractiveness is also attested by successful applications, as PIs to national competitive funding calls (PHRC, ANSM and ANRS grants, 3 ANR grants and 1 ANSES grant) and high recruitment of permanent staff (4 young researchers and 4 technical staff).

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

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

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

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

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

The unit is member of several research groups at the national level (creation and direction of the FHU PREMA, 2020; FHU PaCeMM; FHU SENEC; French group of Faecal Transplantation GFTF). At the European level, the unit is member of the EuroToxemia and Placental groups. The unit is also member of the COMBACTE-CDI consortium dedicated to clinical, diagnostic and therapeutic issues related to *Clostridioides difficile* infection; the deputy director of the unit is the French coordinator and treasurer of this consortium.
During the reporting period, 3PHM has contributed to the organisation of one national meeting ('Groupe de la francophonie Placentaire', GfP – Paris 2019) and five international meetings (Eurotoxemia – Paris 2018, International *Clostridium difficile* symposium, ICDS - 2018 et 2020, European Society for Reproductive Immunology, ESRI – Paris 2022, International Society for the Study of Hypertension in Pregnancy, ISSHP – Montpellier 2022).
The unit has attracted researchers and technical staff; two MCU, one MCU-PH, two AI, one IE, one TN and one full-time researcher (CRCN Inserm) have joined the unit during the reporting period. The unit also has regular recruitment of PhD students (16 over the period) and postdoctoral fellows.
The unit has obtained several competitive national grants during the reporting period. This corresponds to a total amount of nearly 2.25 M€, including European contracts (60 k€), national calls (6 ANR grants, 2 ANSES grants, 1 PHRC grant, 1 ANRS grant, 1 ANSM grant; 1.6 M€) and 'Plan d'Investissements d'Avenir' (PIA) Idex/Labex/Equipex' (650 k€). Most of them were coordinated by members of the unit as PIs: PHRC, ANSM and ANRS grants, three ANR grants and one ANSES grant.
The unit has secured financial support for the recruitment of 7 PhD students (including 3 funded by the French Ministry of Research, exchanges with China, Lebanon), and five postdoctoral fellows (including two from public grants and one from industry (Sanofi)).
Two researchers of 3PHM are members of the 'Académie Nationale de Pharmacie' and one researcher was a visiting scientist in a research centre in India for a period of nearly three years. The young researchers of the unit have also obtained a total of 7 prizes during the period for oral and poster presentations in conferences such as 'Groupe de la francophonie Placentaire' - 2023, 'Colloque Association pour la Recherche en Toxicologie' – 2023, 'Congrès de la Société Française' DOHaD, Targeting Microbiota Congress – 2018.
The researchers of 3PHM are members of several journal editorial boards such as Placenta, International Journal of Molecular Sciences, Journal of Hospital Infection, Hygiènes, and have been guest editors for several special issues in their field of research and expertise (PPAR special issue in International Journal of Molecular Sciences, *C. difficile* special issue in Frontiers Medicine, DOHaD & Microbiota special issue in Frontiers). They are also highly active as reviewers for international journals such as Plos Pathogens, Nature Communications, Journal of Biochemical Chemistry, Life, Journal of Cellular and Molecular Medicine, Clinical and Translational Gastroenterology and Scientific Reports.
The researchers of 3PHM contribute to science evaluation as members of research piloting boards such as HCERES, ABIES Doctoral School of AgroParisTech, and as reviewers for funding agencies such as ANR and 'Groupements interrégionaux pour la recherche clinique et l'innovation'.
The unit includes eight technical laboratory staff who master complementary expertise ranging from biochemistry, molecular biology, microbiology, cell culture, cell biology and cell imaging to mouse experimentation and surgery, providing strong experimental support. The technical staff regularly maintain their skills by training and are also very active in setting up novel technologies within the unit such as the development of organoids, the *ex vivo* placental perfusion in rodents, sequencing and bioinformatics analysis together with cutting-edge microscopy.
The unit has set up an operative strategy for scientific integrity and open science through efficient traceability of raw data and deposit in public databases together with reviewing of all experimental protocols by trained and experienced technical laboratory staff.

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

Although the unit has obtained regular and substantial funding over the reporting period, most of the funding currently available will terminate in 2024 (3 out of the 4 available contracts).

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The scientific production of 3PHM in fundamental and translational research is excellent with 201 original publications in journals of solid reputation (e.g. Gut Microbes, American Journal of Clinical Nutrition, American Journal of Pathology, American Journal of Transplantation, Allergy, Hypertension, Environmental Health Perspectives, Journal of Cellular and Molecular Medicine), both in the fields of placenta and newborn microbiota. The unit's scientific output is impressive, averaging 2.2 publications per scientist per year. PhD students published on average two to three articles in first or second author position.
Moreover, the solid expertise of the unit and its international visibility on pathophysiological placenta development have led to collaborations on placental cellular mechanism promoting foetal demise with an associated publication in a top-ranked journal (Science).

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

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

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

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

The originality of the research activity is based on the complementarity of fundamental and clinical approaches to address crucial scientific questions relating to gestational diseases or disorders associated to gut microbiota dysbiosis, while considering the exposome. This high-quality research is made possible by the high proportion of researchers who are also hospital practitioners and by the combination of different methodological tools (cohort studies, animal models and *in vitro* studies). This research paves the way for the development of innovative early diagnostic approaches (biomarkers) and new therapeutic strategies.
The unit published 201 original articles, among which 63 in last author, 49 in corresponding author and 22 in first author positions. In addition, the unit's director is last author of 52 among these 201 articles. The unit also published over twenty reviews and 7 book chapters. This regular production is of high-quality considering the teaching and hospital functions of most of the researchers.
As highlighted in the portfolio, both groups published in high profile generalist (Nature Communications and Nature Medicine) or speciality journals, including Allergy, American Journal of Transplantation, Environmental Health Perspectives, Gut Microbes, Environment International.
The placentologist group published in the prestigious journal Science in 2019 on the discovery of a key placental cellular mechanism involved in the abnormal development of the placenta, promoting foetal demise. The contribution of the group members (in first and last positions among the authors with equal contribution) reflects their visibility as specialists in placental pathophysiology, enabling collaborations with other researchers.
There is good interaction between researchers with numerous co-authored publications in the unit, but there is only one common publication between the microbiota and placenta groups. All researchers published and most of them published a minimum of one article per year and a maximum of eleven articles. PhD students published on average two to three articles in first or second author position during their thesis.
The contribution of postdocs is valued through publications (mostly in first or second position with certain postdocs as corresponding author).
The scientific production of 3PHM respects the principle of scientific integrity, ethics, prevention of plagiarism and fabrication.

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

There is a moderate proportion (about 9.5%) of original papers in journals published by MDPI (e.g. 3 in Nutrients, 1 in Antioxidants, 3 in Microorganisms, 1 in Nanomaterials, 4 in International Journal of Molecular Sciences, 4 in Journal of Clinical Medicine, 1 in Microbiology Research, 1 in Molecules, 1 in Toxics) in the scientific production of the unit.
The publications of the unit are not systematically updated in HAL repository.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The inclusion of the unit's research in society is excellent. It addresses significant societal and public health challenges, including major obstetrical diseases associated with placenta dysfunctions and the pathophysiological role of intestinal microbiota in premature newborns.

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

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

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

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

The potential to contribute to health care economics is well evidenced through the large number of partnerships developed with the non-academic world, particularly with private companies of the probiotic area: Maat Pharma in 2020–2022 (155 k€), Davolterra in 2021–2022 (35 k€), Sanofi Pasteur (315 k€), Willo (8 k€), Deinove in 2022 and Pileje (2016 – 2018, 160 k€; 2018–2021, 242 k€ and 2022, 172 k€).
There is strong evidence of links with industrial partners, over the translational projects, involving for example biomarkers of obstetrical diseases or possible therapeutic strategy.
The skills of members of 3PHM have also been recognised through several invitations as experts by private companies (Besins, Bledina, Havea) or consulting activities for various companies (Tillots, Pfizer, MSD, Astellas).
The microbiologist group succeeded in isolating many interesting strains: (i) strains able to prevent colonisation by pathogenic *C difficile* in an animal model (patent deposited in 2020 with an application for European extension from 2021); (ii) three strains of Bifidobacteria able to protect from neonatal necrotising enterocolitis lesions; (iii) three other probiotic strains (*Lactobacillus* and *Bifidobacterium*) able to exert preventive effects in a mouse model of cow's milk allergy; (iv) strains of *Bifidobacterium* able to improve *in vitro* and *in vivo* the dysfunctions associated with irritable bowel syndrome.
The unit has a strong capacity to communicate its interests and research findings to the public through media outlets. Members of 3PHM have interactions with 'Le cercle FSER' aiming to establish dialogue between researchers and high school students (DECLICS program), to interest them in the construction of knowledge through meetings with high school students.
Members of 3PHM are implicated in on-line videos or press release information intended to the general public, including 'Interferon et grossesse pathologique' (2019), video 'Hemato'K' 'Diarrhée chez le patient d'hématologie, plateau promotionnel' (2020), video 'Prévention santé', Groupe Edimark Santé (on-line press service reserved for health professionals) COVID-19 (2021), 'Prévention de la dissémination des bactéries multirésistantes aux antibiotiques et actualités sur les infections à *C. difficile*'.

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

Events dedicated to the general public are limited to a few topics and are organised by few members.
Despite identification of probiotic candidates for the management of irritable bowel syndrome, no patents have been deposited.

ANALYSIS OF THE UNIT'S TRAJECTORY

The UMR-S 1139 'Pathophysiology & Pharmacotoxicology of the Human Placenta; pre & postnatal Microbiota' (3PHM), created in 2018, results from the merger of two units: UMR-S1139 'Pathophysiology & Pharmacotoxicology of the Human Placenta' and EA 4065 'Intestinal ecosystem, probiotics, antibiotics'. This combination of expertise, grouped together in the same unit, makes it possible to study: 1/the impact of the environment associated with the mother's state of health (microbiota, pollutants, metabolism, genetic variants, etc.) on the development and functions of the placenta and reproductive function; 2/ the impact of the establishment of the intestinal microbiota on the health of the newborn and the child (allergy, ulcerative colitis, neurodevelopment). The period from conception to the first two years of life, also called the first 1000 days is decisive for the health of the future adult (DOHaD concept).
The organisation of the unit, divided into two axes, placenta and microbiota, reflects this history. The first axis focused on the development and function of the chorionic villi both in normal and pathological pregnancies and the relationship with foetal growth restriction. The microbiota research axis includes the microbiome establishment in the neonate, targeting premature infants and its consequences on the child's health and the development of preventive and therapeutic approaches of gut microbiota dysbiosis.
For these two axes, both basic and translational research are developed, aiming (1) to identify biomarkers of the pregnancy outcome or intestinal disease associated to gut microbiota dysbiosis, such as necrotising enterocolitis, allergies and irritable bowel syndrome and (2) to develop new therapeutic (using probiotics and faecal microbiota transplantation to cure or prevent gut microbiota dysbiosis or nanomedicine to treat pre-eclampsia).
During the reporting period, a project aiming to evaluate the possible contribution of placental microbiota on the gut colonisation has been performed at the interface between the two groups, placenta and microbiota. However, the demonstration that the placenta does not harbour a microbiota has hindered further collaborative research on the placenta. The scientific exchanges between the two groups, facilitated by the organisation of regular meetings, enabled the construction of collaborative projects in progress to explore the relationships between the maternal microbiota, placental functions and the microbiota of the newborn, and the consequences for the health of the mother and child. A study on the impact of maternal gut microbiota dysbiosis associated with severe obesity on reproductive and placental functions, pregnancy outcome and establishment of the newborn's microbiota is now in progress. The first paper on the topic, entitled 'Association between gut microbiota at 3.5 years of age and body mass index at five years: Results from two French nationwide birth cohorts', is now in press.
A new research axis on the effect of minipuberty dysfunction on the female fertility and puberty will be developed with the arrival of an Inserm researcher. Two projects are already funded (2 ANR grants). Il is a real opportunity to connect the expertise of this researcher on female reproductive function to that of the unit on the impact of placental function, pollutants and gut microbiota on child and adult health and disease. This researcher will develop collaborations within the unit, on the role of glycosylation of gonadotropins, on the impact of exposome on minipuberty and subsequent reproductive function and on the relationship between mother and neonate microbiota and the reproductive function. But this ambitious interactive line of research is based on a single researcher.
In conclusion, the research carried out by this unit is based on solid skills, on the development of original models, and on the constitution of pooling cohorts and a national and international collaborative network, enabling it to address relevant questions relating to the impact of the materno-foetal and newborn environment on the health of the newborn and the child.

RECOMMENDATIONS TO THE UNIT

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

The unit is encouraged to undertake all initiatives aimed at reinforcing the social life and the interactions between the two groups.
Even though the welcome and supervision of new arrivals, in particular PhD students, is generally well organised, procedure, contact and booklet for new arrivals regarding safety and psycho-socio risks should be implemented.
The unit's strategy of developing a new research topic on the effect of minipubertal dysfunction on female fertility and puberty, which relies on a single new arrival scientific member, could lead to thematic dispersion and weaken this new research activity. The unit is encouraged to evaluate the reinforcement of this thematic axis and its interactions with the clinical research, or to reconsider this thematic organisation in order to avoid scientific isolation and ensure its successful development.

Recommendations regarding the Evaluation Area 2: Attractiveness

Most of the funding currently available will terminate in 2024. The unit is therefore encouraged in continuing to apply to national and European competitive calls and also to calls from the PEPR project led by Inserm 'Santé des femmes et des couples' as the thematic of the unit is fully in line with this PEPR project, in order to secure the budget for the development of all projects. This point is important, considering the significant increase in staff members over the reporting period.

Recommendations regarding Evaluation Area 3: Scientific Production

All members of 3PHM are encouraged to continue their dynamic scientific output by giving priority to high-profile journals.
The unit could reflect on the choice of journals (as far as possible, non-predatory journals) and make publications more visible by promoting open science by systematically updating publications in HAL repository.

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

The 3PHM unit is encouraged to carry out both basic and translational research. It could go a step further and applies the outcomes of its pathophysiological studies to develop tools to improve the screening, early diagnosis (biomarkers) of pathological gestation or digestive diseases associated to gut microbiota dysbiosis (such as necrotising enterocolitis, allergies and irritable bowel syndrome) and new therapeutic targets (nanomedicine, probiotics, faecal microbiota transplantation…).
The unit has a good potential of research valorisation and could evaluate the possibility of setting up a spin-off or start-up company to meet the demands of the pharmaceutical industry.

CONDUCT OF THE INTERVIEWS

Date

Start: 27 novembre 2023 à 8 h 30

End : 27 novembre 2023 à 18 h

Interview conducted : on-line

INTERVIEW SCHEDULE

8:30-9:00	**Hcéres committee meeting** *Closed-door meeting*
9:00-9:05	**Hcéres rules and procedures *by M. Mercier-Bonin*** *Public session (all unit members)*
9:05-9:55	**Scientific and administrative presentation of the unit** 25 min including unit's trajectory. Overall presentation of the unit *Thierry Fournier & Frédéric Barbut* 25 min. Discussion *Public session (all unit members)*
9:55-10:20	**Committee debriefing and break** *Closed-door meeting*
10:20-11:00	**Meeting with ITAs (in French)** *In the absence of any managing staff*
11:00-11:40	**Meeting with researchers** *In the absence of any managing staff*
11:40-12:20	**Meeting with post-docs and students** *In the absence of any managing staff*
12:20-1:15 p.m.	**Lunch break**
1:15 p.m.-1:55 p.m.	**Meeting with institutions' representatives: Université Paris Cité & Inserm** *Closed-door meeting*
1:55 p.m.-2:15 p.m.	**Committee debriefing** *Closed-door meeting*
2:15 p.m.-2:55 p.m.	**Meeting with the Director & Deputy director of the unit** *Closed-door meeting*
2:55 p.m.-3:10 p.m.	**Break**
3:10 p.m.-6 p.m.	**Committee debriefing & redaction of the final report** *Closed-door meeting*
6 p.m.	**End of the interview**

GENERAL OBSERVATIONS OF THE SUPERVISORS

Université Paris Cité

Le Président

Paris, le 19 février 2024

HCERES
2 rue Albert Einstein
75013 Paris

Objet : Rapport d'évaluation de l'unité **DER-PUR250024157 – 3PHM – Physiopathologie et Pharmacotoxicologie Placentaire Humaine, Microbiote pré & post natal**

Madame, Monsieur,

L'université Paris Cité (UPCité) a pris connaissance du rapport d'évaluation de l'Unité de Recherche **3PHM – Physiopathologie et Pharmacotoxicologie Placentaire Humaine, Microbiote pré & post natal.**

Ce rapport a été lu avec attention par la direction de l'unité, de la part de laquelle vous trouverez un courrier en annexe signalant les erreurs factuelles à corriger (en particulier sur l'intitulé de l'unité), le vice-doyen Recherche et le doyen de la Faculté de Santé d'UPCité, par la vice-présidente Recherche d'UPCité et par moi-même.

Le Doyen de la Faculté de Santé et moi-même souhaitons souligner que cette unité s'intègre dans le paysage de la recherche de l'UFR de Pharmacie, et que ses thématiques scientifiques s'inscrivent pleinement dans la stratégie de la Faculté de Santé, notamment dans le cadre du projet stratégique d'UPCité sur la santé des Femmes. Je n'ai pas par ailleurs d'observations de portée générale complémentaires à apporter.

Je vous prie d'agréer, Madame, Monsieur, l'expression de ma considération distinguée.

Édouard Kaminski

Présidence

Référence
Pr/DGDRIVE/2023

Affaire suivie par
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UMR-S 1139 « 3PHM »
Physiopathologie & Pharmacotoxicologie du Placenta Humain
Microbiote pré & postnatal
Directeur : Thierry Fournier
Adjoint : Frédéric Barbut

Paris, February 7, 2024

First of all, we would like to thank the members of the expert committee for the positive evaluation report on our unit UMR-S1139 (3PHM).

Please find below some additional information to the referee's concerns.

1/ The researcher Céline Guigon (CRCN Inserm) joined our laboratory in November 2023.

- She heads up a new axis (fertility and minipuberty) in line with the unit's new project, which now includes reproductive functions and fertility: "Placental and Reproductive Functions, pre- and post-natal Microbiota" (Fonctions Placentaires et Reproductives, Microbiote pré & postnatal – FPRM).
- She receives technical support from the team: Audrey Chissey (AI, imaging); Marie Léone Vignault (AI, molecular biology); Raja Djelidi (IE, cell culture); Véronique Fauveau (AI, animal experimentation and microsurgery).
- She is currently supervising a PhD student and will be soon hiring an engineer for 12 months (ANR contract).
- With our collaborators at ESPCI with whom we are characterizing the glycoforms of hCG during normal and pathological pregnancies (8 joint publications), we will also study the glycoforms of LH and FSH during development in humans, and in particular during mini-puberty.
- Céline Guiguon will be involved in several projects with placentologists and microbiologists (see below).

2/ We are developing several translational projects at the interface between placentology, microbiology and reproductive functions.

- *In vivo* impact of pollutants (nanoplastics, phthalates, nanoceria, PAH) on placental development and function, foetal growth, gestation outcome and minipuberty in mice (Amal Zerrad Saadi, MCF; Ioana Ferecatu, MCF; Céline Guigon, CRCN; Véronique Fauveau, AI).

- *In vivo* impact of maternal microbiota (dysbiosis) on placental development and functions, foetal growth, gestation outcome and minipuberty in mice (Anne-Judith Waligora Dupriet PRU; Ioana Ferecatu, MCF; Amal Zerrad Saadi, MCF; Céline Guigon, CRCN; Véronique Fauveau, AI).

- We are currently exploring the impact of maternal microbiota (dysbiosis linked to severe obesity) on reproductive and placental functions, the outcome of pregnancy, the establishment of the newborn's microbiota and minipuberty (pilot study: Microbiota Obesity Pregnancy - Thierry Fournier, DR; Marie Léone Vignaut, AI; Frédéric Barbut, PUPH; Julio Aires, PRU)

- We currently investigate physiological function of xenobiotic receptor AhR during trophoblast differentiation with implication of ligands from microbiota (butyrate) and pollution (HAP, dioxin) (ongoing Master 2 internship, Ioana Ferecatu (MCF), Julio Aires (PRU) and external collaboration Xavier Coumoul (PRU)

3/ Several applications for financial support are currently being assessed or will be submitted this year.

Successful applications since the visit:

- *Grant from FHU PaCEMM*: "Evaluation de l'effet de traitements thermique ou chimique ou par filtration des transplants fécaux pour inhiber la croissance de Clostridioides difficile in vitro » (10 k€)

- *Grant from Fondation de France:* "Project EMRA: Early microbiota as a risk factor for autism" (Anne Judith Waligora Dupriet, PRU, 250 k€)

Current applications submitted:

- *ANR ButyNEC* (Preterm necrotizing enterocolitis: linking *Clostridium butyricum* pathogenicity with the disease) (Julio Aires, PRU)

- *ANR PRIMINDEV* (PReterm Infant and gut MIcrobiota: impact of primocolonization in NeuroDEVelopment) (Anne Judith Waligora Dupriet, PRU)

- *ANR CdiffenseRNA* (Roles and interplay between RNA-based defense systems in the interactions of *Clostridioides difficile* with phages) (Olga Soutourina, Frédéric Barbut, PUPH)

- *Bourse Biocodex (projet ABRICO)* (Bénédicte Pigneur, MCUPH, Frédéric Barbut, PUPH) (L'infection *à Clostridioides difficile* est-elle associée à des modifications des profils d'acides biliaires chez les enfants atteints de RCH ?)
- Fondation BINC (projet ABRICO) (Bénédicte Pigneur, MCUPH)
- *Fondation Association Robert Debré (projet ABRICO)* (Bénédicte Pigneur, MCUPH)
- *Fondation FiMATHO (projet ABRICO)* (Bénédicte Pigneur, MCUPH)

- *Fondation BINC:* "Microbiota Obesity Pregnancy" (Thierry Fournier, DR; Marie Léone Vignaut, AI; Frédéric Barbut, PUPH; Julio Aires, PRU)

- *AAP Emergence Univ Paris Cité*: "Glycoforms of hCG for pregnancy follow up" (Thierry Fournier, DR; Nathalie Delaunay, PRU ESPCI)

- *PERP SAMS PRONEOBIO* (Role of probiotics in preventing necrotizing enterocolitis in preterm neonates: inside the mechanisms of action and host-microbiomes interactions) (Nadim Cassir, Julio Aires, PRU; Frédéric Barbut, PUPH)

- *PERP SAMS PSYCHOBIOTICS* (Unravel how early environmental stressors modulate gut microbiota function and affect mental health). Poirté par Quentin Leyrolle, INRAE (nous sommes partenaire)

Crossing Cutting Edges : "Identifying AhR-ligand key to unlock placenta function" (Ioana Ferecatu, MCF; Xavier Coumoul, PRU) 2nd submission

4/ Procedure, contact and booklet for new arrivals

- The prevention officer (Audrey Chissey, AI) trains new arrivals in safety risks.

- Two people from the laboratory (Julio Aires, PRU and Raja Djelidi, IE) are responsible for dealing with psychosocial risks.

This information is now included in the internal rules that all people working in the laboratory, including trainees, must read and sign.

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