

Research evaluation

# EVALUATION REPORT OF THE UNIT Nutriomique – Nutrition et obésités : approches systémiques

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

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

# EVALUATION CAMPAIGN 2023-2024 GROUP D

Rapport publié le 01/03/2024

High Council for evaluation of research and highter education



# In the name of the expert committee<sup>1</sup> :

Philippe Lefebvre, Chairman of the committee

For the Hcéres<sup>2</sup> :

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 President of Hcéres.



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

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

# MEMBERS OF THE EXPERT COMMITTEE

Chairperson:	Mr Philippe Lefebvre Institut national de la santé et de la recherche médicale - Inserm, Lille
	Mr Yves Boirie Université Clermont-Auvergne (representative of CNU section 4404)
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Experts:	Mr Gilles Mithieux Institut national de la santé et de la recherche médicale - Inserm, Lyon (representative of Inserm CSS3)
	Ms Andrea Rau Institut national de recherche pour l'agriculture, l'alimentation et l'environnement - INRAE, Jouy en Josas
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Mrs Camille Chaudonneret, Déléguée Régionale Inserm Paris Ile-de-France Centre Est

Mr Loic Carballido, Directeur Recherche et Innovation, APHP



# CHARACTERISATION OF THE UNIT

- Name: Nutrition and obesities: systemic approaches
- Acronym: NutriOmics
- Label and number: UMR 1269
- Composition of the executive team: Pr. Karine Clément

#### SCIENTIFIC PANELS OF THE UNIT

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

#### THEMES OF THE UNIT

The themes developed by the single team UMR1269 unit are based on an integrative approach to the pathophysiology of genetic and non-genetic severe obesity. This translational research approach seeks to identify the origins of susceptibility to severe obesity, the role of inflammation, fibrosis, and intestinal flora in obesity, and to characterize the impact of metabolic therapies, including bariatric surgery, on these parameters. The unit's strong links with the clinic enable it to implement genome-scale bioinformatics analysis strategies for patient cohorts and to assess the impact of proposed treatments. The unit's activities are divided into five interactive areas: (i) the study of the role of intestinal microbiota in the progression of obesity and associated metabolic pathologies; (ii) the study of the role of adipose tissue remodelling in the progression of obesity and associated metabolic pathologies; (iv) the development and use of bioinformatics 'data integration' tools for the study of systems biology; (v) the clinical applications of the discoveries in areas (i-iv).

#### HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The UMR1269 research unit 'Nutrition and obesities: systemic approaches' (NutriOmics) has been headed by the current director since 2019. UMR1269 has a dual affiliation with Sorbonne University and INSERM. It is the offshoot of an Avenir team established in 2002 by the current director (2002–2006), which then existed as a team in unit U755 at Université Pierre et Marie Curie (UPMC) (2007–2008), within Inserm unit U872 (team 7) at the Cordeliers Research Center (AP/HP Pitié Salpêtrière, CRNH Île-de-France) (2009–2014) and finally in UMR1166 (AP/HP Pitié Salpêtrière, team 6) (2014–2018), culminating in the current structure created in 2019 (Faculté de Médecine, Blvd de l'Hôpital and Hôpital Pitié-Salpêtrière).

#### RESEARCH ENVIRONMENT OF THE UNIT

The UMR1269 research unit is part of a local and regional network of diversified and complementary scientific, clinical and technological expertise. The unit has close links with the nutrition, anatomo-pathology and diabetology departments of the Pitié-Salpêtrière hospital. Global management of cohorts via the Centre National de Recherche en Nutrition Humaine (CRNH) and clinical trials via the Centre d'Investigations Cliniques Paris-Est provides a strong clinical anchor. Local access to the P3S and UMS28 platforms provides technological which is usefully complemented by access to platforms at the Cochin Institute, ICAN and the Brain Institute. The unit and its director have been instrumental in setting up some of these structures (Idex ICAN, CRNH). In line with the 'omics' and data mining/exploitation dimension, the unit has strong historical links with the UMMISCO (Unité Mixte de Modélisation Mathématique et Informatique de Systèmes Complexes, Naturels, Biologiques ou Sociaux) International Joint Research Unit of the Institut de Recherche pour le Développement (IRD). The unit has been/is involved in French (F/CRIN-Force), European and international clinical and/or basic research networks (FP7 Metacardis, IMI2 Litmus) as a coordinator or partner. Finally, the unit is building relationships with large and medium-sized economic players (Danone, Nestlé...).



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

Catégories de personnel	Effectifs
Professeurs et assimilés	9
Maîtres de conférences et assimilés	3
Directeurs de recherche et assimilés	3
Chargés de recherche et assimilés	4
Personnels d'appui à la recherche	12
Sous-total personnels permanents en activité	31
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	8
Post-doctorants	3
Doctorants	9
Sous-total personnels non permanents en activité	21
Total personnels	52

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	С	PAR
SORBONNE UNIVERSITÉ	13	2	10
INSERM	0	5	2
AUTRES	1	0	2
Total personnels	14	7	14



# **GLOBAL ASSESSMENT**

#### Unit description:

The UMR1269 research single team (mono-équipe, five workpackages)) unit, known as 'Nutrition and Obesities: Systemic Approaches' (NutriOmics), focuses on an integrative approach to understand severe obesity, both genetic and non-genetic in origin. UMR1269 is headed by its current director since 2019 and is affiliated with both Sorbonne University (SU) and INSERM. It currently hosts about 60 staff members, with 35 permanent positions (25 from SU, 7 from INSERM, 3 others). The translational research carried out in this unit aims to uncover the factors contributing to susceptibility to severe obesity, the roles of inflammation, fibrosis, and gut microbiota in obesity, and the effects of metabolic therapies, including bariatric surgery, on these aspects. Providing a robust clinical foundation, the unit's collaboration with clinical departments at Pitié-Salpêtrière Hospital allows conducting genome-scale bioinformatics analysis on adult and pediatric patient cohorts (like Pradort and Metacardis) and to assess the impact of proposed treatments. The unit is well connected within a local and regional network of diverse scientific, clinical, and technological expertise.

#### Attractiveness:

The attractiveness and international visibility of the unit are overall outstanding.

Financial resources are mostly from competitive call applications at the European and national levels and industrial collaborations to reach 84% of total funding (salaries for permanent staff are not included in these calculations).

At the international level, the unit is a partner of Fondation Leducq grant (270KE) and obtained a CAPES-COFECUB for 4-year funding of post-doctoral fellows from Brazil. At the EU level, 6/12 grants are coordinated by the unit: FP7-Metacardis (14 partners, 12700kE for the unit), MEDMOTILUS (370kE), ... Nine national contracts out of twelve were obtained as principal investigator: PHRIP DietMed (2089 kE), ANR-CAPTOR (347kE), ANR-PRC-BARIMICE (423kE total), PHRC DRIFTER (400 kE). The unit is also partnered in two RHU (CARMMA and CHOPIN, 1250kE) and obtained the prestigious Equipe FRM label (300kE).

It has also actively participated in various committees, enhancing its integration into the fields of obesity research and its leadership role. The unit maintains a strong scientific reputation, exemplified by its involvement in international, European, and national scientific meetings (Keystone symposium, WOF, and IPWSO) and its receipt of prestigious scientific awards (Jacobaus, Novo Nordisk foundation, Gallien, Fondation Bettancourt-Schuller...). The laboratory has been successful in recruiting 6 young researchers for permanent positions within Inserm and the university, contributing to its vitality. Access to cutting-edge equipment within the lab, as well as in nearby institutions, is available to the unit. Furthermore, twelve PhDs were defended for thirteen HDR in the Unit.

To ensure its leadership position, the unit should consider expanding its BiolT (System biology and data integration) group, as the demand for data storage and innovative analysis is increasing significantly and is vital for staying at the forefront of research. Establishing a policy for regularly updating aging equipment and addressing infrastructure issues, such as the premises at the Faculté de Médecine, could enhance the unit's appeal. Additionally, increasing the number of postdoctoral fellows may be beneficial for a unit of its size. The unit could improve its efficiency by recruiting or securing additional support personnel 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 impact of metabolic health on gut microbiota diversity and functional implications of metabolic diseases associated dysbiosis, the confounding role of medication for metabolic diseases on the gut microbiota composition. Furthermore, other members actively participate in pharmaco-epidemiological clinical studies, overseeing the follow-up of patients experiencing rare obesity and undergoing treatment with novel medications, such as subjects heterozygous for variants in the leptin/melanocortin pathways. 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 313 papers, with 82 of them involving clinical investigators. These papers have garnered a higher-than-average citation rate (ICn:2.1), emphasizing the visibility of their research. Many papers were published in high-profile generalist or speciality journals (Lancet, Nature, Nat. Med., Nat. Comm., Cell Metab., Gut, Diabetes Care...) as first and/or last/co-last authors. The unit also supports innovative research through the development of clinical and research tools while adhering to 3R principles. The unit encourages the participation of both senior and junior Principal Investigators (Pls) in publications, fostering collaboration and increasing research productivity. Technicians and engineers are also contributors to publications, which aids in their career advancement.

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 promotes open science by publishing preprints on open-access repositories and is gradually moving toward a FAIR Data Management Plan (DMP).

However, the division of research topics into separate themes, while closely related scientifically, could potentially hinder more in-depth mechanistic investigations and innovative questions. Additionally, there are cases where the commitment of doctoral and post-doctoral students as first authors in scientific publications is relatively low. To enhance the quality of scientific production, the unit should place a greater emphasis on uncovering fundamental mechanisms of action and increasing hypothesis-driven research, particularly to complement observational projects. To foster collaboration and scientific cohesion within and between themes, it is advisable to reduce the fragmentation of topics and consider merging related areas. The adoption of cutting-edge techniques, including single-cell approaches, in both basic and clinical projects will be instrumental in maintaining the unit's leadership in its field. Furthermore, current and future PIs should explore opportunities to play significant roles within large European and international consortia.

#### Valorization:

The unit has achieved remarkable success in developing predictive tools and introducing innovative concepts in drug development. They have played significant roles in 9 clinical trials related to the treatment of genetic and other forms of obesity, with involvement in coordination and as Principal Investigators. These efforts have fostered strong partnerships with patient associations and health authorities, such as the Haute Autorité de Santé (HAS), aimed at establishing national guidelines for obesity management. The unit has also engaged in collaborations with prominent economic players to evaluate the effectiveness and safety of new treatments through dedicated clinical trials (RHYTHM-Pharmaceutical, Millendo, Novo-Nordisk) or other kinds of activity (consultancy DANONE). In addition to their research endeavours, the unit actively participates in public outreach initiatives (publication of books, articles in newspapers and magazines, webinars, and interviews). However, it's important to note that despite their significant contributions to translational research, the unit has not been actively involved in patent applications and commercial exploitation of their findings. This activity should be expanded to provide additional resources to the lab through increased interaction with SATT and Inserm-Transfert, for example.



# **DETAILED EVALUATION OF THE UNIT**

# A-CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous report stated in 2017 that this research unit is headed by an international leader with outstanding scientific production, highly embedded within international and national networks. It recommended securing access to clinical resources, increase relationships with industry, decrease communication/outreach activities. It also pointed to a (relative) lack of internal organization with respect to finance and administration, health and safety, quality control and research integrity. It also recommended reinforcing PhD and postdoctoral hiring and to stabilize young researchers within the structure. It finally recommended balancing research efforts between themes.

Most of these recommendations have been considered and improved, with the exception of the administrative support which is still virtually absent in the unit. The unit is currently devoting 34.3 FTE to its research activities, 77% of them being involved in fundamental research activity. There is, however, a porosity between research axis allowing researchers and clinicians to contribute to distinct, well-identified themes, thereby ensuring a relative balance between themes. The BioIT axis remains understaffed for the planned workload (3.2 FTE). The unit has efficiently stabilised competences as two full-time Inserm researchers have been recruited, as well as three assistant professor-hospital practitioners (MCU-PH) thus strengthening the translational aspect of research. The flux of PhD students (12 defended theses, 7 in progress) and of postdoctoral fellows (12) supported by national or exchange programs confirms the current strong involvement of the unit in training activities. The administrative/logistic staff was one FTE (who left the unit last year), which was low considering the amount of grants and the increasing staff to be managed, and is as from today clearly insufficient. Other aspects of the life unit (health and safety, quality control and research integrity) are structured around three staff members, and the lab is organized to head toward open science and a FAIR data management plan.

# **B-EVALUATION AREAS**

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

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

#### Assessment on the scientific objectives of the unit

The unit has established scientific goals that range from excellent to outstanding, positioning itself as an international leader in the field of genetic obesities and the development of associated therapeutic approaches. Their active participation in European consortia, like Metacardis, has proven to be highly productive. Additionally, their collaboration with bioinformatics and artificial intelligence group has resulted in the creation of innovative and state-of-the-art tools. To enhance their research, it's important to foster greater synergy within and between themes or work packages, some of which may be overly segmented, to enable more in-depth exploration by mechanistic studies.

#### Assessment on the unit's resources

The unit's available resources are of an excellent standard. The unit, primarily under the name of its director, has very effectively secured approximately 650,000 euros per year through successful applications for international and national grants, ensuring stable operational funding. The influx of new permanent young researchers has brought a highly positive dynamic to the team, allowing them and others to work within a technologically advanced environment, including access to a shared computing cluster at IRD, and fostering close collaboration with clinicians. Access to human biological resources is remarkable. However, the unit faces a challenge due to its limited recurrent funding, which puts at risk the renewal of essential laboratory equipment, such as -80 freezers. Furthermore, the growing demand for substantial data storage and analysis capabilities has become a bottleneck, hindering in-depth exploration of the collected data.



#### Assessment on the functioning of the unit

The unit operates at an excellent level of efficiency. The director is proactive and dynamic, fostering a collaborative and supportive atmosphere among lab members, regardless of their roles, which contributes to a positive working environment. Unfortunately, the continuously increasing normative and administrative workload places a significant and sometimes unequally shared burden on researchers and engineers/technicians, diverting their focus from scientific endeavours, and it appears that there is no imminent relief from this challenge in sight.

#### 1/ The unit has set itself relevant scientific objectives.

#### Strengths and possibilities linked to the context

Within the broad and competitive field of obesity research, the NutriOmics unit tackles with genetic and nongenetic causes of obesity. It has defined three main research topics which are the role of microbiota in obesity, the role of gut in metabolic disorders and the importance of adipose tissue remodelling in obesity. This scientific endeavour is ambitious but is set within a well-defined research program concretized by outstanding publications in each field (among 313 total) in leading generalist and speciality journals (Nature, Nature Med., Gut, Cell Metabolism...). These research axes are deeply intermingled with clinical research, with 26% of papers involving clinicians, and supported by a dynamic bioinformatic group. Clinical aspects also cover the design of predictive tools to which the BioIT group (System biology and data integration) contributes productively, as well as to more fundamental aspects of research. Importantly, the unit participates to or organize the establishment of patient cohorts, a definitive asset in this highly competitive field.

The ongoing research project, which includes notably numerous clinical trials, fits within leading authorities' policy (to which unit members contribute) to decrease the burden of obesity in France. To achieve these goals, the unit was/is integrated as a coordinator or partner within fourteen international (Leducq, CAPES-COFECUB) or European (FP7-Metacardis, IMI2-Litmus...) networks. National networks are integrated through major PIA/RHU-supported grants (2, partner). Important nonacademic players are also brought into play, as shown by the high number of clinical trials (10) coordinated by the unit and collaboration with big pharma and biotechs.

#### Weaknesses and risks linked to the context

Remaining at the forefront of obesity research requires a strong ability to develop and implement a highly integrative and innovative data analysis pipeline. The foreseeable, ever-increasing data (over)load will require more manpower in the BioIT group.

# 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

Human resources in the lab (60 persons) as from today are full-time (Inserm) researchers (6 FTE), professors and assistant professors with (4.4 FTE) or without clinical duties (2.1 FTE), postdoctoral fellows (12 FTE total) and PhD students (18 FTE total, 5 ongoing), technical support staff (engineers, technicians: 7 FTE). The unit, through successful application to grants ensuring revenues averaging 650k€/year, is able to fill non-permanent research positions (mainly postdoctoral fellows and PhD students). The staff is located in two premises (Fac de Médecine, Pitié-Salpétrière hospital) allowing integration of clinical, observational studies with investigational approaches. Technological resources are accessed through 'in-house' equipment ranging from 'basic' molecular biology, biochemistry and cell culture devices to more specialized equipment (anaerobic chambers, Nanopore sequencing, cell sorting, microfluidics) and allow the development of ongoing projects. Local access to sequencing, proteomic, imaging platforms as well as to biobanks are granted through dedicated Sorbonne University platforms, Pitié-Salpétrière clinical departments or nearby institutes (Cochin, Brain Institute...). Highly secure computer resources are coordinated between the unit, Sorbonne University and the UMMISCO team at IRD. Financial resources are mostly from competitive call applications at the European and national levels and industrial collaborations to reach 84% of total funding (salaries for permanent staff are not included in these calculations).



Weaknesses and risks linked to the context

With the ever-decreasing recurrent financial support from governing bodies, the unit is unable to host research staff in decent facilities which may deter prospective collaborators from joining the lab. Space is limited, and lab equipment is getting old. Support from governing bodies is only achievable through multiple, annual calls which are time-consuming. The committee noted that most of the grants (56% total) are allocated to the director unit, reflecting the need for a broader involvement of the unit's researchers in applying to calls.

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 unit is closely monitoring career progression of its members and making the necessary moves to support young researchers (successful) application to Inserm and University permanent positions (5 within 6 years). Promotion of researchers and of technical support staff is also very proactive. An 'assistant de prévention', together with two members of the lab (assistant professor and engineer) are in charge of biological and chemical risk prevention. Access to scientific resources and computer systems is controlled through cryptography of two-level identification systems. Raw data and processed data are stored in distinct places and back-upped regularly.

#### Weaknesses and risks linked to the context

The unit director and the staff are putting a strong emphasis on the psychosocial risks (PSR) induced by the dilapidated premise in the Faculty of Medicine, which are quoted to be close to insalubrity, and acknowledged by Cour des Comptes to be at best obsolete. It also appeared to weigh on students' minds. Of note and following Inserm's initiative, a PSR committee has been formed and closely monitor these issues, concrete actions are yet to follow. The committee noted an excessive burden of administrative and logistic tasks on technicians, engineers and researchers. Safety may be compromised by the lack of investment of monitoring devices and lack of equipment renewal and maintenance. The unit has not defined a common policy for safeguarding experimental data in a way compatible with further valorization.

#### EVALUATION AREA 2: ATTRACTIVENESS

#### Assessment on the attractiveness of the unit

The unit's appeal is exceptional. It is demonstrated by a high level of dynamism and success in both organizing and participating in international networks and consortia such as Leducq, EU IMI, and Metacardis, as well as national initiatives like PHRC and RHU. This dynamic approach is also evident in the unit's ability to organize prestigious meetings like Keystone symposium, WOF, and IPWSO. The unit has recently recruited six young researchers for permanent positions and actively mentors both national and international students from countries such as Brazil and Poland. At the local level, the unit's collaboration with hospital departments provides access to highly valuable adult and pediatric cohorts, as seen in initiatives like Pradort and Metacardis, which is a significant asset.

However, this high visibility and appeal are d threatened by the unit's hosting conditions, as it currently lacks the space for further expansion and faces challenges related to deteriorating premises.

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 has long been committed to the establishment and development of national and European research networks. Through the coordination and/or participation to European SABs, other committees or research networks (Novo-Nordisk, EASD, FP7, IMI2) as well as national endeavours in the obesity field (development of clinical tools Obsgen, Diarem; coordination/participation to networks such as FCRIN/FORCE), the unit has built on these efforts to be integrated in the European and national obesity field and to maintain its leadership position. The unit has a high scientific reputation which is exemplified by the organization/involvement in international (Keystone), European (EASD) and national (AFERO, SOFFCO) scientific meetings (6), and by receiving 7 prestigious scientific prizes (Jacobaus, Gallien, Fondation Bettancourt-Schuller...).

The laboratory has been very active and successful at recruiting young researchers on Inserm (2) and University (3) permanent positions.

The unit has been very successful at coordinating or participating to highly competitive international and european (Metacardis, IMI-Litmus, Leducq) and French research (RHU, 2) consortia. It has obtained 33 grants from charities and other french agencies.

The unit has a secured access to a large panel of cutting-edge equipment within the lab itself or located in the hospital or nearby institutes (Cochin, Brain Institute). Of note, access to human biological resources is also ensured at the local level and allows leveraging large cohorts of patients with obesity undergoing bariatric surgery (n>3,000), to pediatric and adult forms of rare obesity (PRADORT cohort) and to the european Metacardis cohort (n=2,150).

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

The unit should pay a specific attention to increase its BioIT group as demand for data storage and analysis are increasing exponentially and are critical to remain on the cutting-edge of research. A lab policy to regularly renew aging equipment should be defined to avoid obsolescence. Attractiveness is also limited by degraded premises at the Faculté de Médecine, which may deter motivated foreign scientists to join the lab. Along these lines, the number of postdoctoral fellows is quite low for such a large unit.

#### EVALUATION AREA 3: SCIENTIFIC PRODUCTION

#### Assessment on the scientific production of the unit

The scientific production of the unit is excellent. It attests to long lasting and sustained research efforts in the field of obesity that have yielded top-tier original scientific publications and reviews over the evaluation period. This excellence also translates to the level of the French Health Authority (HAS), for which members have contributed to highly commended recommendations for health professionals. Improving the relative lack of porosity between and within topics/axis would propel the unit's research to even higher standards by facilitating in-depth investigations and harmonizing the heterogenous production across work packages.

- 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

Since its inception, the unit has set up a highly productive research program investigating energy and metabolic perturbations in obesity. Combining human genetics and other exploratory approaches to unravel mechanisms leading to obesity-induced abnormalities, the unit has published seminal contributions to the understanding of the role of gut, microbiota, pancreas, adipose tissues and the interaction thereof in disease progression.



Altogether, members of the unit have published 313 papers in the last five years, 82 of them involving clinical investigators and with a higher-than-average citation rate (ICn=2.13, PDC papers: ICn=2.09). These numbers emphasize the high visibility of the research. Many papers were published in high-profile generalist or speciality journals (Lancet, Nature, Nat. Med., Nat. Comm., Cell Metab., Gut, Diabetes Care...) as first and/or last/co-last authors. Innovative research is supported by the development of clinical or research tools (scoring systems, organoids, organ on chips), the latter ensuring compliance with 3R rules. Senior and junior PIs are equally associated to publications, and thematic interactions increase researcher productivity index. Of note, technicians and engineers are also associated to publications, giving them a momentum for career advancement. The rate of participation to international or national scientific meetings through oral communications and posters (300) despite the COVID pandemics is excellent and increases the unit's visibility at the international level. The unit is abiding to the Open science rules as much as possible, by publishing preprints on open-access repositories. Through a specific organization, the unit is slowly evolving toward a FAIR DMP.

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

The deliberate fragmentation into themes/axis/topics, although very closely related from a scientific point of view, may hinder more in-depth mechanistic investigations and innovative questions. The commitment of doctoral and post-doctoral students to the scientific production as first authors is in some cases low.

#### 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 within society is outstanding. The unit has forged strong links with industry through clinical trials of drugs and other types of lifestyle interventions. It has revealed the economic potential of its discoveries in the prevention and treatment of genetic and non-genetic obesity. The dissemination of its expertise in the business world, and among national decision-making bodies, as well as toward the non-specialized public through various media is intense. Financially, the return on investment seems beyond what might legitimately be expected. Continued development of these societal links, through increased awareness about data valorization, should undoubtedly provide additional support for the laboratory's research activities.

- 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 unit had outstanding successes in developing new predictive tools and bringing new concepts to drug development, combined with its involvement (coordination: 1; PI:34) in clinical trials for the treatment of genetic or of other obesities. This implied strong relationships with patient association and health authorities (Haute Autorité de Santé, HAS), with whom the unit is collaborating to set national guidelines for obesity management. Strong interactions with pharma companies are also engaged to assess new treatment efficacy and safety during dedicated clinical trials (9). Lay public outreach is also actively developed through books and newspapers/magazines, webinars and interviews.

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

It is noteworthy that despite an outstanding bench-to-bedside research, the unit has not been active in patent applications and exploitation.



# **ANALYSIS OF THE UNIT'S TRAJECTORY**

Originally organized around a single team structured into five workpackages, the unit is set to transform into a two-team entity. The core research themes from the previous setup will remain intact, with the 'data integration, modelling, and Al' themes, which is considered essential for data analysis and integration, ultimately serving as a central hub for both teams. The first team will be under the leadership of the current director, and each research axis will be co-led by a pair consisting of a junior and a senior scientist, combining clinical and biological expertise. The new team, led by E. Gauthier, who has a long-standing history of collaboration with the current unit, is expected to infuse the unit with new energy, introducing the immunometabolic dimension and promoting the adoption and advancement of cutting-edge techniques such as single-cell RNA sequencing (scRNA-seq) and mass cytometry throughout the entire unit. The committee supports the overarching goal of nurturing emerging team leaders from team 1, alongside a gradual merging of related research axes. It is recommended to expand the focus of some axes to encompass critical physiological mechanisms and encourage more indepth mechanistic studies. The committee acknowledges and encourages further initiatives in the field of clinical research, particularly emphasizing nutritional approaches, a much-needed perspective in this domain. Maintaining and strengthening the connection between clinical and fundamental approaches is considered a significant asset of this laboratory.



# **RECOMMENDATIONS TO THE UNIT**

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

The unit would benefit from hiring or obtaining support staff to handle administrative, financial, and logistical tasks, with the goal of simplifying internal procedures related to ordering and administration. Similarly, there is a need to strengthen the bioinformatics and statistics work package by appointing a dedicated engineer. The responsibility for grant applications and student mentoring (PhD/HDR) should be expanded to include WP/axis leaders. To enhance access to training, it is advisable to identify a 'correspondant de formation' (CoFo). Furthermore, there should be a greater and ongoing dialogue with governing bodies regarding health and safety issues, which should be prioritized when applying for related Sorbonne University infrastructure grants.

#### Recommendations regarding the Evaluation Area 2: Attractiveness

The need for lab space qualitative and quantitative improvement should be urgently considered. It is recommended that English be adopted as the primary communication language during lab meetings. Additionally, efforts should be made to enhance the visibility of younger Pls as current or prospective leaders of WPs. Promoting the dissemination of innovative bioinformatics tools developed within the unit for broader use within the scientific community will underscore the culture of innovation within the unit.

#### Recommendations regarding Evaluation Area 3: Scientific Production

The heterogeneity of the scientific production points to the need for improving the focus of some themes. This can be achieved by strengthening efforts to uncover fundamental mechanisms of action and by increasing hypothesis-driven research to bolster observational projects. To promote scientific cohesion and collaboration within and between themes, it is advised to minimize the 'fragmentation' of themes, including the merging of related topics. Embracing state-of-the-art techniques, such as single-cell approaches, in both basic and clinical projects, will help maintain the unit's current leadership position in its field. In addition, it is recommended that current and future PI) consider strengthening or establishing leadership within large European and international consortia.

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

It would be beneficial to enhance collaboration with SATT and Inserm-Transfer to encourage additional activities related to technology transfer and commercialization.



# **TEAM-BY-TEAM OR THEME ASSESSMENT**

Name of the supervisor: Clément et Aron-Wisnewsky

# THEMES OF THE GROUP

The group studies the link between intestinal microbiota and the progression of (cardio)metabolic disorders, with a focus on obesity. During the past period, several links between so-called 'dysbiotic' intestinal microbiota patterns and metabolic diseases have been fortified. The group has specifically contributed to knowledge on the impact of metabolic health on gut microbiota diversity and functional implications of metabolic diseases associated dysbiosis, the confounding role of medication for metabolic diseases on the gut microbiota composition and gut microbiota transfer models in mice to research causality.

# CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The recommendations were to focus on originality in models and approaches in this very competitive field of research, to safeguard the group's innovative capacity and international leadership. For this, interaction and coherence of the different groups were pointed out as a main factor. In the current organization chart, this seems to be considered as both group leaders are also involved in research activities from groups 3 and 5, and there is a substantial overlap with activities in group 4 for both a post-doc and a research engineer.

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	2
Sous-total personnels permanents en activité	5
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	0
Post-doctorants	2
Doctorants	3
Sous-total personnels non permanents en activité	7
Total personnels	12

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

# EVALUATION

#### Overall assessment of the group

This is a world-leading group which produces key papers in a highly competitive international context. As such, the group has a high international visibility with output in top journals. Overall, this is an outstanding group that achieves a high-level output given its size.

#### Strengths and possibilities linked to the context

The group (8.5 FTE) has a high international visibility with output in top journals. Over the past period, eight papers have been published and one patent has been filed. The group invested in the recruitment of new clinical

**Workpackage 1:** Progression of obesity and related complications: role of gut microbiota



cohorts, in-house metagenomic sequencing and IA-derived prediction for diabetes resolution. Three PhDs have been defended in this group over the past period and one is ongoing.

#### Weaknesses and risks linked to the context

The group is lacking a full-time (senior) researcher. The number of postdoctoral staff is also limited. The diversity in research subjects further involves risks and might hamper the group to stay at its high international level. The new structure that is being laid out for the upcoming period is in line with advancing insights in the field, however, the expected growth of the group and the diversity of subjects, involves risks and might hamper the group to stay at its high international level.

#### Analysis of the group's trajectory

This internationally renowned group aims at further expanding. In a first axis, along to research on nutrition, microbiota and metabolic health, additional research lines are being set up. It is planned to assess the value of additional microbiota samples from other niches to evaluate metabolic health, as well as to focus on additional mouse models to study causality, using notably microbiota transfer. Four additional axes are being set up within the same group. Together they integrate the current Nutriomics expertise in a promising way.

# RECOMMENDATIONS TO THE GROUP

The new structure that is being laid out for the upcoming period is in line with advancing insights in the field, however, the expected growth of the group and the diversity of subjects, involves risks and might hamper the group to stay at its high international level. Specific research focuses are recommended to stay at the forefront in research.



#### Workpackage 2:

Ribeiro et Serradas

# THEMES OF THE GROUP

Name of the supervisor:

The group addresses three main themes. The first is entitled 'perturbations of enteroendocrine cells in metabolic diseases', the second 'perturbations of intestinal permeability in human obesity' and the third 'perturbations of pancreatic islet homeostasis in link with obesity /inflammation / immunity & rescue mechanisms'.

Intestine as a key player in metabolic disorders

# CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The recommendation of the previous report was to increase the workforce of the group by recruiting doctoral and/or postdoctoral fellows. This recommendation has been fulfilled, since one PhD student and one postdoc fellow are present. The recommendation to increase the interactions with the pharmaceutical industry is more difficult to evaluate.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	3
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	1
Sous-total personnels permanents en activité	7
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	1
Doctorants	1
Sous-total personnels non permanents en activité	2
Total personnels	9

# **EVALUATION**

#### Overall assessment of the group

The group has developed several research themes which were (1) gut GLP1 endocrine system and sweet taste signalling in the context of type 2 diabetes (with 2 publications: Osinski et al. Int J. Obes 2021; Le Gléau et al. AJP-Endocrinol Metab, 2021); (2) intestinal permeability in human obesity (1 publication: Genser et al. J. Pathol 2018) and (3) the development of a surrogate gastric bypass that increases pancreatic insulin content (1 publication: Amouyel et al., EBioMedicine 2020). The production is satisfactory. Some studies are translational, but most of the work is essentially descriptive. The overall assessment for this group is very good.

#### Strengths and possibilities linked to the context

The two main strengths of this group are (1) its long-standing knowledge of the gut endocrine system and its staff composition, which mixes scientific researchers and clinicians. This facilitates translational research, addressing questions in both mice and humans, as illustrated in the following publications: Genser et al., 2018 and Amouyel et al., 2020.



#### Weaknesses and risks linked to the context

The first weakness of the group is its limitation in terms of workforce, with five teachers researchers (including 3 with clinical duties) and only one full-time researcher, plus one post-doctoral fellow and one PhD student. The number of full-time researchers in the group is therefore insufficient to ensure rapid data acquisition. The second weakness is the descriptive character of the work produced during the period of evaluation. Finally, an important area of investigation (the role of the gastrointestinal neural system) is not considered, despite the fact the nervous system has an important role regarding intestine endocrinology and intestine-pancreas interactions. The group members acknowledged that they should improve their expertise in the field.

#### Analysis of the group's trajectory

The trajectory of the theme seems rather incremental for each researcher involved. An investigation that takes into account the essential aspect of intestinal physiology is recommended.

# RECOMMENDATIONS TO THE GROUP

It is recommended to the group to make all necessary efforts to attract full-time researchers. One mean could be to increase the activity in training PhD students and post-doctoral fellows, who could then postulate for permanent positions at French research organisms. Accordingly, the number of participants in the group being low, we suggest abandoning some projects and concentrating on fewer questions.

Efforts must definitely be made to improve the dynamism of research, in particular by raising specific questions and implementing mechanistic approaches.

Finally, given the group's focus on intestinal endocrinology, it is recommended that members deepen their knowledge of the gastrointestinal nervous system and its role in controlling glucose and energy homeostasis, so that they can apply this knowledge in their future research plans.



#### Workpackage 3:

Adipose tissue remodelling

Name of the supervisor: Dugail et Marcelin

# THEMES OF THE GROUP

The investigations of the group are focused on the adipose tissue and its remodelling in obesity, fibrosis and aging. The objectives are two-fold: (1) to characterize the molecular and cellular actors contributing to the adipose tissue dysfunction in severe obesity and (2) to identify targets to reverse dysfunction and to prevent weight rebound after weight loss. The research themes, expertise and approaches of both group leaders are complementary with molecular and cellular biology together with metabolism, autophagy.

### CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The recommendation 'to strengthen the group through new recruitment, in particular increasing the number of PhD students (or post-docs)' has been considered since one post-doc has been recruited in 2023 as INSERM researcher and two PhD students and 4 post-docs have been/are in the group (1 PhD for the previous report). The recommendation 'to strengthen interactions with the other themes in order to maintain momentum, productivity and attractiveness' have been taken into account as a group leader is also involved in group 1, investigating the links between ceramides and phosphatidylglycerols, gut dysbiosis and adipose tissue remodelling and glucose metabolism, with two publications and co-authorships in Gut microbes in 2022.

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

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

# EVALUATION

#### Overall assessment of the group

The research of this group on adipose tissue fibrosis is acknowledged by three recent reviews in journals of high reputation (Annu Rev Physiol. 2022; Rev Endocr Metab Disord. 2021; J. Clin Invest 2019) and investigations on autophagy with the development of an original mouse model (published Autophagy, 2020) and on the anti-fibrotic effects of Betahydroxybutyrate in mouse cells (published in Mol Metab, 2022). An original mice model overexpressing adipose lysosomal lipase has been developed (Diabetes, 2020). Adipose tissue senescence has been investigated within the frame of RHU CARMA (Circulation 2018, Diabetologia 2020, Aging cell 2021). This group has a very good to excellent productivity on a relevant health issue, backed up by an important network of collaborators.



#### Strengths and possibilities linked to the context

The strengths of the group are the complementary expertise and approaches developed by both group leaders and the recruitment of a young researcher with additional expertise on mitochondria-derived metabolites and lipids (glutamine and phosphatidy|glycerols). The network of collaborators and success in obtaining funding establishes a ground for relevant research themes.

#### Weaknesses and risks linked to the context

The weaknesses of the group are (1) few interactions with the other groups from the unit to promote translational approaches (for example, no implication in the adipose tissue fibrosis scoring developed in group 1) and (2) few interactions within the group itself, with only one publication with both group leaders as co-authors (Autophagy, 2020). Visibility may be difficult to improve due to highly competitive research themes in the field, and the committee notes few invitations and participation in congresses and seminars.

#### Analysis of the group's trajectory

The group's trajectory appears to be ascendant with the recruitment of a new INSERM researcher. Of note, one of the current group leaders will change for the next mandate. The research theme will focus on the fibroinflammatory phenotype, with an original and promising focus on the impact of metabolic rewiring on chromatin remodelling. The two other proposed axes on collagenolysis and sensitivity to catecholamines seem to be more related to the involvement as partners in two ANRs than to any original contribution from the group. To maintain the leadership in the research on adipose fibrosis, it is advisable to avoid the multiplication of ancillary projects.

### RECOMMENDATIONS TO THE GROUP

The committee issues the following recommendations: (1) interactions with other groups of the unit should be increased to foster translational approaches, (2) the unity and visibility of the group should be improved and (3) develop state of the art and original approaches to remain at the forefront of adipose tissue fibrosis research.



#### Workpackage 4:

Systems' biology and data integration

Name of the supervisor: Sokolovska et Soula

# THEMES OF THE GROUP

This transversal axis works in close connection with the other axes in the unit to develop and implement analytical tools based on statistical/machine learning and mechanistic approaches. Primary methodological contributions focused broadly on (1) stratifying patients based on metagenomic data analysis using metabolic networks; (2) establishing and validating interpretable predictive scores for clinical outcomes using machine learning and artificial intelligence techniques; and (3) providing support for statistical analyses of heterogeneous omics data.

# CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Previous recommendations were as follows. (1) Tools (especially for metagenomic data) developed within Axis 4 are likely to be of wide interest. To ensure their visibility and use, it would be wise to implement a more proactive strategy of diffusion and valorisation via community-specific platforms (GitHub, website, etc.). This recommendation has been partially followed. Some of the novel developed methods are indeed available as open-source code on GitHub (e.g., Predomics from Prifti et al., 2020; open-source Python code from Zendrera et al., 2021 and Zendrera et al., 2019) but these implementations have not been highlighted in the report or on the Tools tab of the unit's webpage. (2) The activities of this axis require computing resources (CPU/GPU) and storage space. The group should be vigilant about the evolution of this technical infrastructure to be sure of being able to efficiently support the unit's work and more particularly the development of sequencing on MinION (Oxford Nanopore). The mutualized HPC cluster with the IRD UMMISCO group seems to address this recommendation, and the group plans to reconfigure the HPC cluster architecture to make it more robust and scalable as a five-year deliverable.

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

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

# **EVALUATION**

#### Overall assessment of the group

Group 4 is clearly a highly valued part of the unit and has been integral for many of the landmark results achieved by the lab. This can notably be seen by the fact that IA, metabolism/microbiome analyses and integrative approaches are highlighted as scientific achievements of the lab, particularly with respect to contributions to guide clinical decision-making. The group has developed novel approaches for predictive models, patient stratification and integrative multi-omic analyses for interpretable biomarker identification, and it has solid expertise in state-of-the art omics analyses. The overall assessment is excellent.



#### Strengths and possibilities linked to the context

Group 4 has been able to capitalize on scientific questions raised within the unit to identify impactful areas of methodological development. This is testified not only by the procurement of ANR grants related to these topics as coordinator (1) or partner (1) and publications (2) in leading bioinformatic journals (Gigascience, BMC Bioinformatics), but also by mutualized projects (8) and co-authorships in 37 generalist (Nature, Nature Med., eLife...) or speciality (Gut, Metabolomics, Autophagy...) journals. These contributions have been realized by maintaining strong ongoing ties with IRD via the participation of associated researchers, as well as through pertinent external collaborations with respect to artificial intelligence approaches.

#### Weaknesses and risks linked to the context

The number of members/FTE in group 4 is small with respect to the importance of its transversal axes to the unit's research objectives and the increasing size of available high-throughput data that must be analyzed. Group 4 members with expertise in biostatistics/bioinformatics may be somewhat isolated thematically from their scientific communities, although the close ties with IRD-UMMISCO and the Sorbonne Center for AI may mitigate this risk.

#### Analysis of the group's trajectory

Since the last evaluation, the size of the group has been fairly stable, and previous strengths noted (interdisciplinarity, interface with other axes, expertise) have been maintained. Group members have contributed as leaders (first or last authors) to bioinformatics/biostatistics publications, and as collaborators to applied publications in the unit led by other axes. The trajectory appears to be positive and fairly linear. The recently funded ANR project Deepintegromics (2021–2026) coordinated by JD Zucker will further reinforce the group's visibility in deep learning for precision medicine.

### RECOMMENDATIONS TO THE GROUP

Given the importance accorded to axis 4 for the unit's achievements, recruitment in this area is needed to reinforce the group and ensure sustainability in statistical support for the unit activities as well as maintenance/transfer of expertise within the unit. The axis may consider reinforcing internal teaching/training activities to share expertise about specialized analyses and method development activities. Given the risk of thematic isolation for group members with biostatistical/bioinformatic expertise, it is important to maintain ties with these communities (e.g., existing methodological networks) and strike a balance between methodological developments and support for applied research. Although the axis has to be congratulated for making efforts to provide open-source implementations of developed methods (GitHub links within papers), these could be centralized on the unit website and better highlighted as research output of the unit to reinforce visibility and encourage methods reuse by a broader community.



#### Workpackage 5:

Translating our fundamental research for the benefit of patients

Name of the supervisor: Poitou et Dubern

# THEMES OF THE GROUP

In this group, most of the studies have been performed on the translational aspects of the scientific approaches investigated in the lab. It has been mainly focalised on two topics, i.e. bariatric surgery and severe and genetic obesities. Strategies for improvements in metabolic phenotypes and comorbidities were proposed and new care management, notably using new drugs, have been explored.

### CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The very strong complementarity and synergy between clinical research, experimental research and bioinformatics approaches, has been fully respected and even strengthened during the past years through outstanding achievements. The innovative research advances have always been directed toward applications to the patient's care.

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

Catégories de personnel	Effectifs
Professeurs et assimilés	5
Maîtres de conférences et assimilés	3
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	3
Sous-total personnels permanents en activité	11
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	0
Post-doctorants	3
Doctorants	0
Sous-total personnels non permanents en activité	3
Total personnels	14

# **EVALUATION**

#### Overall assessment of the group

This axis is highly successful in translating results obtained in previous studies and from other group activities into clinical practice for the benefit of patients. Conversely, clinical research and implementations of patient cohorts are regularly used to support more fundamental research. The main objectives to develop innovative diagnosis, phenotyping and discover new predictors and secondly to develop innovative therapies, is fully achieved. The development of innovative approaches has been successful and very productive as reflected by numerous clinical trials. The overall assessment of this group is excellent to outstanding.

#### Strengths and possibilities linked to the context

The group strategy is strongly supported by the solid expertise of the group which includes many clinicians, hence establishing outstanding relationships between the different hospital departments and the basic science performed in the research unit. Through many collaborations with international experts in the field, the group is involved in European projects and has been able to improve diagnostic impasses of genetic obesities and to improve care methodologies. Some members actively participate in pharmaco-epidemiological clinical



studies, overseeing the follow-up of patients experiencing rare obesity and undergoing treatment with novel medications such as subjects heterozygous for variants in the leptin/melacocortin pathways which have been discovered by the same research group more than twenty years ago. Other new drugs under recent development (bi-(GIP/GLP-1) or tri-agonists (GIP/GLP-1/glucagon) of GLP-1 are a new area of research with important clinical consequences in routine care. Clinical trials of new co-agonists for the therapy of obesity and type 2 diabetes are also coordinated by the group.

The clinician-scientists of NutriOmics have coordinated recommendations for the management of obesities (national care programs of the French National Authority for Health, HAS). They are involved in the coordination of care networks and teaching in Rare Disease Centers and in European meetings for the training of colleagues. In relation with the basic research activities and with their positions within international scientific societies, clinician-scientists have been involved in the coordination and in working groups of 7 HAS recommendations regarding the management of obesity, diabetes and of metabolic surgery as well as in the organization of national and European meetings targeted on these research aspects and on care pathways.

#### Weaknesses and risks linked to the context

The development of clinical trials based on new drugs assays is partly dependent on French regulations acceptance. The capacity to rapidly establish new cohorts of patients may be challenging. This is, however, a hurdle commonly faced by all French units in the field of obesity and type 2 diabetes. Translation of findings to patient care may also be limited, especially when regarding drug reimbursement rules and indications for equitable access to treatments.

#### Analysis of the group's trajectory

The strength of the axis 5 of 'Nutriomics' unit is based on a unique and very strong complementarity and synergy between clinical research, experimental research and bioinformatics approaches. The members of the group are strongly involved in academic teaching and training through research and the achievements of the group over the last few years have been remarkable. The trajectory is in line with these past achievements and will include novel promising nutritional strategies to enhance current therapeutic approaches. With this shift, care should be taken to maintain interactions with the more basic aspects of research in the unit.

# RECOMMENDATIONS TO THE GROUP

The remarkable organization and the outstanding quality of basic as well of clinical work is a solid guarantee for keeping a high standard of excellence. Maintaining the human and financial resources to face the major challenges of novel therapeutic approaches is a great challenge for the future as well as an exciting opportunity for the group. Particular attention must be paid to mobilise sufficient human resources to ensure the successful attainment of the established objectives.



# CONDUCT OF THE INTERVIEWS

#### Date

**Start:** 25 octobre 2023 à 8 h 30

**End:** 25 octobre 2023 à 18 h 30

Interview conducted: online

### INTERVIEW SCHEDULE

8:30 a.m8:45 a.i 8:45 a.m9:25 a.i (20 min presenta 9:25 a.m9:45 a.i r ( 9:45 a.m. h-10h0!	<ul> <li>n. Presentation of the committee</li> <li>n. Highlights of the Unit and brief description of the trajectory by the Director</li> <li>tion, 20 min questions)</li> <li>n. Workpackage 1 – Progression of obesity and related complications: role of gut</li> <li>nicrobiota? (Clément et Aron-Wisnewsky)</li> <li>10 min presentation, 10 min questions)</li> <li>Workpackage 2 – Intestine as a key player in metabolic disorders (Ribeiro et Sarradas)</li> <li>10 min presentation, 10 min questions)</li> </ul>
10:05 a.m10:30	a.m. Coffee break
10:30 a.m10:50 ^ (	<b>a.m.</b> Workpackage 3–Adipose tissue remodelling in obesity, fibrosis and aging (Dugail et Aarcelin) 10 min presentation, 10 min questions)
10:50 a.m11:10	a.m. Workpackage 4–Systems biology and data integration (Sokolovska et Soula)
( 11:10 a.m11:30 (	10 min presentation, 10 min questions) <b>a.m.</b> Workpackage 5–Translating our fundamental research for the benefit of patients Poitou et Dubern)
(	10 min presentation, 10 min questions)
11:30 a.m11:50 (	a.m. A new team for the future (Gautier) 10 min presentation, 10 min questions)
<b>12h-13h</b>	Closed-door meeting of the committee
13h-1:30 p.m.	unch break
1:30 p.m2:10 p.i // / 2:15 p.m2:45 p.i	<ul> <li>n. three parallel sessions</li> <li>Aeeting with the technicians and administrative staff (Lead: S. Ventéo)</li> <li>Aeeting with PhDs and post-docs (Lead: A. Bouloumié)</li> <li>Aeeting with researchers not team leaders (Lead: G. Mithieux)</li> <li>n. Meeting with representatives of the local institutions</li> </ul>
2:45 p.m3:15 p.ı	n. Closed-door meeting of the committee
3:15 p.m3:45 p.ı	n. Coffee break
3:45 p.m4:15 p.ı	n. Meeting with the Director
4:15 p.m6:30 p.ı	n. Closed-door meeting of the committee

#### PARTICULAR POINT TO BE MENTIONED

No\_particular point to be mentioned.



# GENERAL OBSERVATIONS OF THE SUPERVISORS



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

à

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

Paris, le 26 janvier 2024

Objet : Rapport d'évaluation Nutriomique - Nutrition et obésités : approches systémiques

Cher Collègue,

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

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

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

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

tot

Sorbonne Université Cabinet de la présidence. 4 place Jussieu, 75005 Paris Email : presidence@sorbonne-universite.fr The Hcéres' evaluation reports are available online: www.hceres.fr

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