

EVALUATION REPORT OF THE UNIT
MASCOT – Marqueurs cardiovasculaires en
situation de stress

UNDER THE SUPERVISION OF THE
FOLLOWING ESTABLISHMENTS AND
ORGANISMS:

Université Paris Cité,
Institut national de la santé et de la recherche
médicale - Inserm,
Sorbonne Université,
Université Sorbonne Paris Nord,
Centre national de la recherche scientifique –
CNRS

EVALUATION CAMPAIGN 2023-2024
GROUP D

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In the name of the expert committee¹ :

Ms Cecile Vindis, Chairwoman of the committee

For the Hcéres² :

Stéphane Le Bouler, acting president

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

Ms Cécile Vindis Institut national de la santé et de la recherche médicale - INSERM

Ms Helene Beloeil Centre hospitalier universitaire de Rennes - CHU RENNES (representative of CNU)

Mr Benjamin Grenier-Boley Institut Pasteur Lille (supporting personnel)

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Mr Freddy Odille Institut national de la santé et de la recherche médicale - Inserm

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REPRESENTATIVE(S) OF SUPERVISING INSTITUTIONS AND BODIES

Inserm IT TS Marie Josephe Leroy Zamia

Université Paris Cité : Doyen Faculté santé : Pr Matthieu Resche-Rigon, VP recherche : Michel Vidal ; Doyen UFR médecine : Philippe Ruszniewski ; Directrice du pôle Recherche et Innovation de la faculté de santé : Christine Guillard

Université Sorbonne Paris Nord : Pascale Molinier

CHARACTERISATION OF THE UNIT

- Name: Marqueurs cardiovasculaires en situation de stress
- Acronym: MASCOT
- Label and number: UMR 942
- Number of team: 2
- Composition of the executive team:

SCIENTIFIC PANELS OF THE UNIT

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

THEMES OF THE UNIT

The 'Cardiovascular Markers in Stressed Conditions' (MASCOT) unit (UMR-S-942) INSERM/Université Paris Cité, Université Sorbonne Paris Nord) is a research unit composed of 2 teams + ATIP-AVENIR team (since 2021).

Team 1: 'Biotargets for cardiovascular dysfunction', Team 2 'Cardiovascular Oncology' and ATIP-Avenir Team 'Immuno-inflammation of the critically ill patient'.

The unit's research main topic is dedicated to translational research in biomarkers. MASCOT unit aims at identifying new biomarkers and biotargets derived from biomarkers as well as innovative biotherapies in cardiovascular disease, cancer and cardio-oncology.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The MASCOT unit is a merger of the former UMR-S 942 and UMR-S 1165, restructured in 2 teams, with an additional ATIP-Avenir team led by B Chousterman (contract for 2021–2024). The unit MASCOT is located in Lariboisière Hospital for team 1 and ATIP-Avenir and Université Paris Nord (Bobigny 93) for team 2. Team 1 and ATIP-Avenir are housed on the 2nd and 3rd floors of Viggo Petersen building in Lariboisière hospital. MASCOT occupies 350 m² of offices and laboratory space, and shares an additional 350 m² with the UMR-S1275. Team 2 has 180 m² of space located at the main Campus of Université Sorbonne Paris Nord (USPN) since 2018.

RESEARCH ENVIRONMENT OF THE UNIT

In Lariboisière Hospital, MASCOT has connections with the CRB (biobank) and with the Clinical Departments, especially Emergency Room, Cardiology or Anesthesia, surgery and critical care units and Research Units of Lariboisière Hospital. MASCOT unit shares common research platforms with the three units of the site. They also adopted a policy to allow a mutual organization of human resources.

At Lariboisière, MASCOT has recently acquired equipment for transcriptomic and single cell analyses. At USPN site (2nd floor) the Team 2 benefited from their own histology facility (cryostat, microtome, confocal microscopy and laser microdissection).

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

Catégories de personnel	Effectifs
Professeurs et assimilés	21
Maîtres de conférences et assimilés	3
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	34
Sous-total personnels permanents en activité	61
Enseignants-chercheurs et chercheurs non permanents et assimilés	12
Personnels d'appui non permanents	2
Post-doctorants	3
Doctorants	24
Sous-total personnels non permanents en activité	41
Total personnels	102

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	24	0	13
AUTRES	7	0	24
UNIVERSITÉ SORBONNE PARIS NORD	7	0	2
INSERM	0	4	4
SORBONNE UNIVERSITÉ	1	0	0
Total personnels	39	4	43

GLOBAL ASSESSMENT

The Unit MASCOT is composed of two teams + ATIP-AVENIR team (since 2021) and is recognized for its excellent level of expertise in the discovery of biomarkers in acute cardiac care and biotargets of cardiac dysfunction as well as innovative biotherapies in cardiovascular disease, cancer and cardio-oncology.

The scientific objectives of the unit are excellent: the unit develops a translational research strategy by combining fundamental, preclinical and clinical research in two fields of cardiovascular and oncology medicine. The scientific objectives of the unit are ambitious but realistic with regard to the expertise and the disciplinary field of the researchers as well as the exceptional local environment. The unit's resources are excellent with a marked increase, each year during the contract from 400 K€ in 2017 to 1,600 K€ in its own financial funding (as PI in regional clinical trial projects PHRC, Chaire Péri-OP, Fondation de France, PEPR Santé numérique, or partner in ANR, ERA-PERMED URICov.), patents and industrial contracts (as PI with Abbott, Roche Diagnostics, Servier, Sanofi) for a total of 5143 Keuros during the five-year period in addition to its recurrent allocation (1548 Keuros). However, European and international funding as PI remain low compared to national funding.

The functioning of the unit is excellent; the annual unit seminar outside Paris, where young researchers have the opportunity to present their work is very well appreciated by all the unit members since they are geographically spread in two sites (Lariboisière and Bobigny). The gender parity of team leader is also improving for the next contract: Team 1 will be headed by a young INSERM woman researcher and Team 3 will be co-headed by a woman PU-PH.

The attractiveness of the unit is outstanding: the unit has been proactive in its attractiveness policy by recruiting two INSERM permanent researchers and two assistant professors and they welcomed one ATIP-Avenir Team (since 2021). Several international postdocs (from Japan, Vietnam and Switzerland) as well as young clinical researchers have spent their internships in the unit. For their clinical research activities, the unit has access to the digital infrastructure (EDS) developed by the AP-HP which allows storing and analyzing biobanks in a secure and efficient way.

The scientific production is excellent with high numbers (1330 original articles, publications, 40% in leading position) in high-profile generalist journals in leading position (i.e. Lancet 2022) and most of them in speciality journals (Eur Heart J, Circ Res, Br J. Anaest, Anaest Critl Care & Pain Medicine, J. Clin. Oncol, Eur. Oncol, Clin. Cancer Res...). The publications of the MASCOT unit are highly cited with the nomination of the Director as 'Highly cited researcher' by Clarivate analysis in 2021 and 2022.

The contribution of research activities to society is excellent since the unit has collaborations with ten pharmaceutical industries (Abbott, Philips, Roche, Sanofi, Servier...) and filed eight patents and one received the Best Innovation Award from AP-HP. The clinical valorization is strong, as assessed by the involvement in guidelines in the field of cardiology and anesthesiology and clinical trials for the industry (STRONG-HF, AdrenOSS2...). Some members of the unit interact actively with patient associations (Action Contre les Spondylarthropathies, FPRIC — Association Française des Polyarthritiques et des Rhumatismes Inflammatoires Chroniques), as a board member and participation to meetings. Senior members of both teams contributed to public symposiums/events to promote research ('Science, Policy & Society', breakfasts of 'Sauvez la vie'), and members were often invited to TV shows during the COVID crisis. Overall the global assessment of the unit is excellent.

DETAILED EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

- 1) **Researchers from team 1 and team 2 should further ally by applying for cooperative grants:** there is no joint funding applications.
- 2) **The initiatives to stimulate interactions between the administrative, technical and scientific personnel of the two teams should be undertaken:** There is an annual unit seminar outside the lab where young researchers have the opportunity to present their work and a renown French researcher is invited to give a talk and his/her appreciation of the scientific quality of the unit.
- 3) **MASCOT should favour the recruitment of researchers/clinicians of all specialities (cardiology, oncology, anaesthesiology and intensive care, pathologists) to preserve the diversity of specializations within the unit:** the unit has recruited two young permanent CRCN INSERM researchers and two assistant professors. A PU-PH joined the MASCOT unit with a new field of research in circulatory failure and immunology and get the ATIP-Avenir grant in 2021. The unit hired mathematicians and engineers to keep developing more multidisciplinary approach.
- 4) **More attention should be paid to internal communication, involving all members of the team (from technicians to supervising researchers. Install team building days on a regular basis, both 'scientifically organized' as well as 'leisure organized', to stimulate intellectual and scientific interactions between both teams, located on a different campus:** there is an annual unit seminar outside the lab where young researchers have the opportunity to present their work.

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 the unit are excellent: the unit develops a translational research strategy by combining fundamental, preclinical and clinical research in two fields of cardiovascular and oncology medicine. The unit has set up new multidisciplinary collaborations (mathematicians and engineers) to develop its research topics. They have a fruitful international collaboration with Vietnam National Cancer Hospital and Hanoi faculty of medicine.

Assessment on the unit's resources

The unit's resources are excellent with a marked increase (each year during the contract, from 600 K€ in 2017 to 1400 K€ in 2022) in its own financial resources (regional, national or international grants, patents and industrial contracts and funded clinical trial projects) 5143 K€ during the five-year period in addition to its recurrent budget (1548 K€). However, there is an imbalance between the funding obtained by Team 1 (4,635 K€) and Team 2 (518 K€) during the evaluation period.

Assessment on the functioning of the unit

The functioning of the unit is excellent, indeed significant efforts have been made to improve team cohesion given the unit's geographical location on two sites (through annual seminars, videoconferencing of unit meetings) but which remains a weakness for the unit, the gender parity is also on the way to improvement.

1/ The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

The scientific objectives of the unit take into account the scientific policy of the site and the strategic orientation plan of the regulatory authorities. The unit is located in very close vicinity of the clinical facilities of the APHP hospitals (Lariboisière for team 1 and ATIP-Avenir team and Avicenne for team 2) which represents an excellent environment to reach their scientific objectives in terms of data integration (e.g. biobanks), biological samples and data storage and processing via the data warehouse of the Entrepôt de Données de Santé of APHP (EDS). The unit has set up new multidisciplinary collaborations (mathematicians and engineers) to develop its research topics. They have a fruitful international collaboration with Vietnam National Cancer Hospital and Hanoi faculty of medicine with the creation of the 'Translational Cancer research Center' in Hanoi and welcoming students (PhD, Postdoc) from Vietnam as well as thirteen co-authored publications, eight invited conferences and three co-organized conferences.

The societal impacts and the innovation of its research policy are attested by its research axis: the project BioADM biomarker led to a Phase II clinical trial in septic shock patients, the design of a new antibody for the treatment of brain metastases from HER-2 breast cancer was patented with Inserm Transfert.

Weaknesses and risks linked to the context

The ratio between full-time researchers and clinicians is still rather low: 37 clinicians (PH, PU-PH and MCU-PH) for 6 permanent researchers (CR, DR and IR) but improving (recruitment of a permanent INSERM researcher during the last mandate and one at CSS7 Inserm in 2023). The dual geographical location of the unit (Bobigny and Lariboisière) could be a brake to the development of the unit's scientific objectives and the unit's cohesion. Several scientific objectives (gold nanoparticles to target cancer stem cells and the genetic link between cancer and chronic inflammation) of the unit rely on high-risk projects (only 1 permanent researcher in Team 2) which might represent a potential threat.

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 unit is staffed with members having either permanent research positions (INSERM CR/DR and CNRS DR), or hospitalo-university bi-membership (PU-PH, MCU-PH), or university valence (PU, MCU, engineer, technicians) or hospital valence (PH) facilitating ongoing interactions between basic and clinical research.

The increase of human resources with permanent positions (+ 1 CRCN (+1CRCN in 2023), + 2 MCU, + 3 PU-PH, + 1 engineer UPC), and the appointment of an ATIP-Avenir team (2021–2024) have contributed to the driving force behind the evolution of the unit.

The unit's resources are excellent with a marked increase in its own financial funding (regional clinical trial projects PHRC (PI), national ANR (partners), Chaire Péri-OP (PI), Fondation de France (PI), PEPR Santé numérique (PI) or international grants FP7 Homage, ERA-PERMED URICov (partners)), patents and industrial contracts as PI Abbott, Roche Diagnostics, Servier, Sanofi) 5143 Keuros during the five-year period in addition to its recurrent budget (1548 Keuros).

The unit has an excellent research environment with access to shared research platforms (histology and imagery), equipments (single cell transcriptome analysis, qPCR) and animal facilities. They have access to the data Warehouse of Health Data stored in the EDS (Etablissement des données de Santé) of APHP to manage and analyze several biobanks.

Weaknesses and risks linked to the context

There is a marked imbalance between the funding obtained by Team 1 (4635 keuros) and Team 2 (518 keuros) during the evaluation period 2017–2022 that could be a risk to ensure the sustainability and ambition of Team 2's research activities.

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 structured into three teams (the ATIP-AVENIR is considered as a team) and headed by a director and a deputy director; the core facility of the unit is represented by research support and permanent research (1 CR) members. Two administrative assistants are present at each site to support researchers and students. Every newly hired person is introduced during weekly lab meeting and has a supervisor appointed. There is an annual unit seminar where young researchers have the opportunity to present their work and a renown French researcher is invited to give a talk and his/her appreciation of the scientific quality of the unit. Three permanent researchers of the unit are in charge either of students (Licence, Master 1 and 2) or post-doc researchers. The unit appointed two parity referents in 2021.

Clinical protocols and trials are performed after approval by all required committees and in compliance with national and international requirements. All the programs are approved by the Ministry of Agriculture after validation by the Charles Darwin n° 5 ethics committee. Ten members of the unit have a valid training in animal experimentation. All PhD students are trained for animal experimentation. Four members of the unit participate in the animal welfare structure (SBEA) of the Lariboisière site. Three researchers are members of the ethics committee in animal experimentation CEEA n° 9 for Lariboisière site, one researcher is a member of the animal welfare structure (SBEA) of the SMBH site, and a member of the ethics committee in animal experimentation (CEEA) Paris Nord n° 123. Two researchers are members of the steering committee of the animal facility. The unit has access to the EDS of APHP to store and analyze several biobanks which complies with security for this type of personal data.

Weaknesses and risks linked to the context

Gender parity is very low with 58 women and 92 men during the last five years which could be improved. Women are under-represented as leaders or co-leaders of the new three presented teams (2 women and 8 men). Moreover, among people having an HDR, there are only 7 women for 27 men. There is no information on the unit's environmental impact and its policy to cope with.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The unit is excellent with the recruitment of two CRCN Inserm, one ATIP-Avenir Team, and two assistant professors. The unit also attracted five international post-docs (Switzerland, Japan) as well as clinical researchers (from CHU Nancy, Nantes). The unit has developed a unique platform/dataware house. However, all competitive grants have been obtained as partner from European (FP7; ERA-Permed) and National institutions (INCA-partner; Chaire IA APHP-PI) leading to a significant increase of overall Unit resources. Although the unit is part of two European grants but they are not principal investigators of these projects.

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

1) The unit has a scientific reputation, both at national and European levels, documented by its fruitful publication record that is among the top rank in the respective scientific and clinical areas as PDC: Lancet, Circ Research, Intensive Care Med, Eur J Heart Fail.

The current director of MASCOT was cofounder of Institute hors-murs ('beyond the walls') 'Institut des sciences cardiovasculaires' launched by the Université Paris Cité in 2021. The Fédération Hospitalière Universitaire (FHU) PROMICE is led by the current director of MASCOT and a Senior INRIA researcher director. MASCOT is founder and executive of the INI-CRCT (part of F-CRIN). INI-CRCT is a multidisciplinary national network with French leaders in the cardio-renal field.

2) The unit has a highly successful recruitment of two CRCN Inserm researchers and welcomed an ATIP-Avenir team in the last funding contract. The unit has welcomed several post-doc researchers (15 Post-doc for Team 1, none for Team 2) and PhD students (31 for Teams 1 and 11 for Team 2) as well as the frequent visits by international Post-Doc (Japan, Switzerland) and Pre-Doc level students at the international level (e.g. from Japan or Vietnam). MASCOT unit welcomed two senior researchers (from North Carolina, USA), highly recognized methodologists and statisticians. Several members of MASCOT have been elected at the national University levels in Research Committee or Executive Committee at Université Sorbonne Paris Nord or Université Paris Cité.

The director is Vice-Dean of International Affairs of the Faculty of Health of Université Paris Cité. MASCOT is involved in Master 1 (Santé publique) and is leading a Master 2 in Inflammation.

3) The unit has a very good level of attractiveness regarding participation in competitive calls such as two ANR as partners, two participation at European contract (FP7, ERA-Permed), documented for example by the successful hosting of a highly competitive ATIP-AVENIR group. Since MASCOT obtained the 'Chaire Péri-OP', the group of 'digital twins' got all authorizations and has full access to the data generated by all operating rooms and surgical ICU in Lariboisière.

4) The unit has access to shared histology and imagery platforms as well as excellent equipment such as the single cell transcriptome analysis. Permanent engineers manage some of these equipment and train the staff and students. Each site of the unit has access to animal facilities along with their dedicated training on animal experimentation. Through collaboration, the unit has access to the EDS (Etablissement des données de Santé) of the APHP which allows storing and analyzing biobanks in a secure and efficient way.

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

Although the unit is partner of two European grants and one INCA, they are not principal investigators of these projects. The unit points out that some of the platforms they have access are rather old which would need some new investments to acquire or have access to newer ones. Except for animal facilities, equipment and platforms are not equivalent between the two sites which might complicate the conduct of some experiments.

Regarding the other references, essentially no major weaknesses or risks could be named.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The scientific production of MASCOT unit is excellent with high numbers (more than 800 publications with 40% PDC: Team 1:557 and Team 2:260) and quality in high-profile generalist (Lancet) and journals of speciality (Circ Research, Intensive Care Med, Eur J Heart Fail).

The publications of the MASCOT unit are highly cited with the nomination of the Director as 'Highly cited researcher' in 2021 and 2022 by Clarivate analysis.

Most first authors of the publications of the unit are either PhD students or postdoctoral fellows.

- 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

1) The scientific production of MASCOT unit is more than 800 publications (Team 1:557 and Team 2:260) including for Team 1, 492 original articles, 56 reviews and 9 guidelines between 2017 and 2022. Most publications were published in in high-profile generalist journals (i.e. Lancet 2022 as first author for the Director) and speciality journals (Eur Heart J, Circ Res, Br J Anaest, Anaest Critl Care & Pain Medicine, J. Clin. Oncol, Eur. Oncol, Clin. Cancer Res...). The unit members are PDC for 40% of the total publications.

The publications of the MASCOT unit are highly cited with the nomination of the Director as 'Highly cited researcher' in 2021 and 2022 by Clarivate analysis as they are already the reference publications in demonstrating major discoveries.

The publications have reported the discovery of new biotargets derived from biomarkers in cardiovascular disease, oncology and in cardio-oncology. Clinical application and benefits have already been shown; i.e. the anti-adrenomedullin biotherapy was shown to have clinical benefits in septic shock. Indeed, the unit demonstrated the genetic link between chronic inflammatory diseases and cancer (Clinical Cancer Res, 2019) or the benefits of starting early and intensively oral heart failure medications in patients ready to be discharged from an acute heart failure episode (Lancet, 2022). Another strength is the publications based on large database acquired in the operating room or in intensive care units.

2) All members (including postdocs and PhD students) of the MASCOT unit are publishers.

3) PhD students are required to take 100 hours of training during their formation, 1/3 of this time is dedicated to research integrity and ethics. Researchers, students and staff involved in research are informed on the principles of honesty, trust and integrity; Aware of the responsibility to comply with high and ethical standards in the course of their research; encouraged connecting with LORIER program from INSERM and using Labguru digital notebook. Scientific manuscripts undergo anti-plagiarism verification.

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

There are no weaknesses and risks linked to the context.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

The interactions with industry are outstanding and are opening opportunities of economic valorization through eight patents (1 licensed), as well as the involvement in clinical valorization through guidelines and clinical trials. Dissemination is also excellent with the organization of online events. However, no start-up was set up.

- 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 has fruitful collaborations with industry (Abbott, Philips, Roche, Sanofi, Servier, Biotem, Innate Pharma, Sherpa engineering, H4D, etc.) resulting in thirteen collaboration research contracts among them twelve as PI for the unit MASCOT.

The unit filed several patents (7 from team 1, 1 from team 2), one of which received the Best Innovation 2021 award of APHP and was licensed.

The clinical valorization is assessed by the involvement in guidelines in the field of cardiology and anesthesiology (9 by team 1), in high-impact clinical trials for industry (STRONG-HF, AdrenOSS2...), with a member of the unit in the board, and interactions with 'Associations de patients' (ACS — Action Contre les Spondylarthropathies, FPRIC — Association Française des Polyarthritiques et des Rhumatismes Inflammatoires Chroniques).

The unit has organized symposiums and online events for young researchers or for the general public, including 'Biomarkers of the future' (team 1, 1000+ attendees), 'Cancer diagnostic strategies' MOOC (team 2, 3000+ attendees each year).

Senior members of both teams contributed to public symposiums/events to promote research ('Science, Policy & Society', breakfasts of 'Sauvez la vie',...) , and two researchers were often invited to TV shows regarding the COVID crisis.

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

Dissemination to the public may still be improved.

ANALYSIS OF THE UNIT'S TRAJECTORY

Since the previous contract, the unit has grown and has been enriched with the arrival of new young researchers, physicians and mathematicians. In the future organization of the unit MASCOT, the current leader of Team 1 will be the Director of the new unit assisted by a deputy Director who is the current leader of Team 2. The renewed unit will be re-organized in 4 teams, including the ATIP-AVENIR team. Team 1 will be split in two teams: Team Biomarkers, Pathophysiology and Therapeutics strategy of cardio-circulatory failure (CIRCUS) for which the leaders will be two young INSERM researchers and respect the gender parity; the research activity for the next years will be focused on defining new targets for biotherapies according to two axis: 1) Biomarkers, Pathophysiology and Therapy in cardiac dysfunction and 2) Biomarkers, Pathophysiology and Therapy in Circulatory failure. The other team is Team Digital twins for peri-operative medicine for which one of the leaders is the future Director of MASCOT, the research axis will be dedicated to advancing perioperative care by developing digital biomarkers and leveraging artificial intelligence by creating a digital platform, combining physiological insights with innovative approaches to digital biomarker design and forecasting. The renewed Team 2 will be renamed: Team Biotargets for metastatic oncology and links with inflammatory diseases, for which the leaders respect the gender parity and are oncologist and rheumatologist PU-PH. The scientific project for the next contract relies on three axes: 1) genetic link between cancer and chronic inflammation; 2) biomarkers of metastatic disease and blood-brain barrier; 3) cancer therapy using gold nanoparticles targeting resistance to antiangiogenics. The fourth team which is the current ATIP-AVENIR (funding goes until 2024, a two-year extension can be requested) Immuno-Inflammation of critically ill patients has two research axes: 1) Role of tissue macrophages on tissue damage and repair during acute inflammation and 2) Immunophenotyping and immunotherapy of the critically ill patient.

Overall, the proposed trajectory of the unit is very pertinent with regards of the acquired expertise on biomarkers and to the evolution of medicine and patient handling with the burst of digital technologies. One concern about the workforce of the renewed Team 2 is that there is only one permanent INSERM researcher for the next contract (1 DR). There is a risk of not having sufficient full-time human resources to implement the project and supervise young researchers. One of the major assets of the unit is the diversity of the profiles of the researchers and their complementarity, which leads to real translational research.

RECOMMENDATIONS TO THE UNIT

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

A written, documented protocol on how to proceed in case of psychosocial conflicts and related problems need to be included in the 'Welcome Booklet' that each new employee will receive. The management of the unit's IT equipment which is now handled by an engineer and a permanent researcher must be handled or subcontracted by a person dedicated to this task.

Recommendations regarding the Evaluation Area 2: Attractiveness

The unit should try to be a more frequent coordinator of major national competitive projects (ANR), or as far as possible of European or international grants.

Recommendations regarding Evaluation Area 3: Scientific Production

The unit is encouraged to continue publishing in high-profile journals, with one recommendation being to continue increasing the number of publications in high-profile generalist journals.

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

The unit is encouraged to increase its dissemination activities to the public.

TEAM-BY-TEAM OR THEME ASSESSMENT

Team 1: Bio-cibles des dysfonctions cardiovasculaires
 Name of the supervisor: Ms Feriel Azibani

THEMES OF THE TEAM

Team 1 is focused on optimising the management of patients with cardiovascular dysfunction with biomarkers, including digital non-invasive biomarkers. The team investigates new targets and defines new biotherapies especially in acute conditions. They demonstrated the benefits of biomarker-guided.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

- 1) The committee recommends focusing on high-impact journals, rather than on high number of papers. The previous recommendations were fully addresses as Team 1 has published 492 articles between 2017 and 2022 in best speciality journals (Cir Res, Eur J of Heart Fail) and generalist (Lancet) as PDC.
- 2) Communication with technical and administrative personnel should be optimized if necessary. All PhD students systematically follow training in the first year of their PhD Thesis.
- 3) The team should focus on mechanistic pathways of biomarker-related effects in vivo. The team has taken into account this recommendation by conducting studies to better understand the metabolism of certain biomarkers and how to optimally exploit them. The team should be aware of the risks of using too many transgenic animals. This issue has been taken into account as among the missions of a newly recruited staff member is to monitor this use.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	11
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	2
Personnels d'appui à la recherche	26
Sous-total personnels permanents en activité	39
Enseignants-chercheurs et chercheurs non permanents et assimilés	10
Personnels d'appui non permanents	1
Post-doctorants	3
Doctorants	20
Sous-total personnels non permanents en activité	34
Total personnels	73

EVALUATION

Overall assessment of the team

The team is excellent with regard to: the innovative project such as the proof and concept of the use of immunotherapies in critically ill patients and the use of artificial intelligence to help physicians in their clinical practice, the attractiveness to young researchers (PhD, two Inserm CRCN recruited), the scientific production (Team 1 published 492 articles between 2017 and 2022 in high-level speciality journals (Cir Res, Eur J of Heart Fail) and generalist (Lancet) as PDC and one member was highly cited researcher in 2021 and 2022 by Clarivate analysis, the translation towards clinics, and the academic partnerships, and one ongoing licensed patent. However, European and ANR grants obtained are not under the lead of the team.

Strengths and possibilities linked to the context

The team expertise in translating research towards effective therapies is well established by means of several research programs that contributed to deepening knowledge regarding pathologies and therapies mechanisms (for example in heart failure). The team is currently conducting activities towards developing digital health – digital models, AI-based cardiovascular and cerebral biomarkers, in particular in the context of operating room and intensive care unit (ICU).

The team has published, during the relevant period, 456 original papers, 51 reviews and 9 guidelines (79% of these peer-reviewed papers were published in speciality journals in the field of anaesthesia, critical care and cardiovascular diseases) were published in speciality journals such as:

Br J Anaesth., Crit Care., Am J Respir Crit Care Med., Heart Fail., Eur. Heart J., Int. Care Med., Clin. Chem., Cir Research...). The team has also published a collaborative clinical study in high visibility journal The Lancet (2022) as first author.

One member of the team was Highly cited researcher in 2021 and 2022.

The team participated to major guidelines by scientific societies such as European Society of Cardiology (ESC) and Heart Failure Association.

PhD students and postdocs represent an important part of the first authors in published papers (49 as first author, 128 as co-author) and all of them present their results in national, European and international meetings at least once a year. Some of them were awarded conference prizes during international meetings. Permanent members of the team are regularly invited to international conferences such as congresses of the ESC, the American Heart Association and the International Symposium on Intensive Care and Emergency Medicine.

They are also involved in the organization of international scientific events (for example, on behalf of the ESC). They are also involved in Editorial Boards (JACC, ACCPM) and in local, national and international steering bodies. Members of the team received prizes: 'Médaille de l'ordre du mérite', Binet Prize from 'Fondation pour la Recherche Médicale'.

The team is attractive to young researchers and has recruited very recently two CRCN Inserm as well as three MCU-PH. The team has also benefited from one 'Poste d'accueil Inserm' in 2021 and has received fifteen post-docs (5 foreigners from Japan and Switzerland).

The team is well funded (about 4M€) and has several partnerships with leading industrials (Abbott, Philips, Radiometer, ...) and is only partner for national competitive calls (PHRC, 2 ANR).

The team develops academic cooperation at national, European and international level and is thus also a partner of two research programs including EU. The team has deposited five patents and has conducted five clinical trials.

Weaknesses and risks linked to the context

Even if the majority of published papers are in the best journals of speciality, there is a low number in high visibility journals for the basic science.

The contribution issues from international and EU contracts: none as PI.

The surface dedicated to the laboratory is relatively reduced and there is a lack of some modern platforms.

The number of permanent basic science researcher is increasing but is still relatively low.

The team modestly contributes to knowledge and sciences dissemination towards the general public.

Analysis of the team's trajectory

The team for the future contract will be split in two teams.

Team Biomarkers, Pathophysiology and Therapeutics strategy of cardio-circulatory failure (CIRCUS) for which the leaders are Ms Ferial Azibani & M Nicolas Vodovar (both Inserm CRCN).

The research activity for the next years will be focused on defining new targets for biotherapies and two main axes will be considered: 1) Biomarkers, Pathophysiology and Therapy in cardiac dysfunction and 2) Biomarkers, Pathophysiology and Therapy in Circulatory failure.

The overall objectives of the team CIRCUS are to identify additional novel biomarkers, understand their pathophysiology, and see their potential role as innovative therapies for cardiovascular and circulatory dysfunction.

Team Digital twins for peri-operative medicine for which the leaders are M. Etienne Gayat & M Fabrice Vallée. This Team will be dedicated to advancing perioperative care by developing digital biomarkers and leveraging artificial intelligence by creating a digital platform, combining physiological insights with innovative approaches to digital biomarker design and forecasting, to allow enhanced practice of perioperative medicine. The main objectives are thus: (i) collecting and processing real-time data from the operating theatre (ii) building a digital twin that models the heart, vessel, and brain crosstalk under general anesthesia, and (iii) using data collected during anesthesia to identify phenotypes associated with poor cardiovascular or cerebral trajectories.

The proposed trajectory is very pertinent with regards of the acquired expertise and to the evolution of medicine and patient handling with the burst of digital technologies and the opportunities that they may offer for healthcare.

RECOMMENDATIONS TO THE TEAM

The team should better identify research items to be prioritized with regards to workforces and timelines. The team should pay attention to potentially increasing external solicitations regarding collaborations and identify ways to selecting the most appropriate ones.

The team has the scientific and technical potential to leading EU research programs and thus increasing incomes from EU Calls.

The team has the ability to contribute to knowledge spreading towards the society and citizens.

Team 2: Bio-cibles de la maladie métastatique en oncologie
 Name of the supervisor: Mr Guilhem Bousquet

THEMES OF THE TEAM

The main subjects of team 2 involve cancer metabolism, cancer therapeutic resistance, therapy cardiotoxicity, and cancer biomarkers to target brain metastasis

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

1) Collaboration with senior researchers from team 1 in the MASCOT Unit should be continued and intensified since to make the proposed research successful: joint funding applications and collaborative projects between teams 1 and 2, which would be highly desirable.

A joint application to PLBIO call in 2023 is described between team 2 and the ATIP-Avenir.

2) The team should consider alternative research hypotheses, like epigenetic mechanisms instead of mutations. The team should further focus on high-risk projects with the potential to gain high scientific return and breakthrough findings, with publications in top-ranking journals.

The team has developed an innovative approach with meta-analysis of genomic data of different cancer types to better approach the prevalence of genetic mutations. The team focus in an individual approach to study the genetics of low penetrance and the links between cancers and chronic inflammatory diseases.

The team has created a bi-disciplinary PhD program, which has already successfully been established (Mathematics, Chemistry). A clear focus and priority ranking of the very demanding working program is essential.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	10
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	8
Sous-total personnels permanents en activité	22
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	5
Sous-total personnels non permanents en activité	8
Total personnels	30

EVALUATION

Overall assessment of the team

The team 2 is assessed as very good due to its scientific output in speciality journals of high international visibility (143 publications, five highly cited papers, 52 in PDC (J. Clin. Oncology, Eur. Oncology, Clin. Cancer Res., Blood)), a clear translational and socio-economic strategy (1 patent issued with Inserm Transfert), and attractiveness in terms of national recruitment (24 trainees and 17 master students), two associate professors (MCU) joined the team, and international level which resulted in the creation of the 'Translational Cancer Research Laboratory' in Hanoi (Vietnam) and 4 co-direction of PhD with Vietnam. The number of PhD thesis defended is low compared to the number of HDR (18).

Funding of the team is low with only one INCA obtained as co-PI, 95 k€), and no competitive national or international grants were obtained as PI during the evaluation period.

Strengths and possibilities linked to the context

One of the great strengths of team 2 is the clear translational focus dedicated to metastatic cancers and inflammatory diseases, with a very successful track record at combining basic and clinical cancer research. Team 2 demonstrated the increased risk of brain metastases in patients with melanoma and that PROM2 expression is biomarker in metastatic lymph-nod, they published a very important systemic review and meta-analysis on the genomics of renal cell carcinoma, they developed a proof and concept for the clinical development of an anti-HER antibody for the treatment of breast cancer overexpressing HER2 (industrial collaboration with Biotem).

During the period, the team published 143 articles in peer-reviewed journals in well recognized journals as first, last or corresponding author (Clin Transl Med, J Clin Oncol, Clin Cancer Res, etc.). Some collaborative papers are highly cited, and one paper is associated with a patent.

Eight PhD theses have been completed and PhD students have publications as a first author.

Team 2 complies with an incentive policy 'Open Science' type HAL. Senior team members have duties in the university and in the board of national societies and work groups.

Moreover, the team created a highly successful DIU in 2021. Team leader launched a very productive international collaboration with Vietnam (experiments taking place in Vietnam, biobanks in France and Vietnam and students trained in the MASCOT Unit to obtain their PhD) which resulted in the creation of the 'Translational Cancer Research Laboratory' in Hanoi.

One member of the team received a prestigious prize, the National cancer hospital of Vietnam for the franco-vietnamese collaboration.

Funding of the team is very low with only one competitive grant (INCA) obtained as co-PI for 95 k during the evaluation period.

There are proven and well-documented collaborations with partners on the national and international (Vietnam, China) level. These cooperations hold the potential to intensify the scientific exchange, and to successfully also participate in international funding programs. The attractiveness of the team is supported by the participation in invited international conferences, the organization of scientific events, such as three French Vietnamese conference cardio-oncology meetings of the SFC, and 'Forum Européen Coeur Exercice et Prévention', and numerous collaborations with both academic (Vietnam, China, Cuba, Columbia, Italy) and industrial partners (Biotem, Innate Pharma, Sherpa engineering, H4D etc.). In particular, the team has a long history with Vietnam, which has led to the creation of a Translational Cancer Research lab in Hanoi in 2019 (co-headed by the team leader), biobanks, joint publications, joint scientific events, and exchange of students/staff. Technicians are involved in publications and are given opportunities for promotion (one promotion to IR). Three members passed the HDR degree during the last mandate. The team has a policy of pooling research funds. Animal research is in compliance with regulations. Open science implementation is in line with the institutional guidelines, and Labguru is used as an electronic lab notebook.

Weaknesses and risks linked to the context

The number of PhD students (5 during the mandate) is low regarding the number of members holding the HDR (18), especially with the permanent Inserm researchers, although this is partly explained by health issues for one of them.

Funding is surprisingly modest compared to the scientific output, as documented by the publication record. In particular, the total amount of funding raised by national and/or international calls (1 INCA obtained, 95 k€) is very low.

Generally, the link between both research sites, which are physically distant, is still difficult.

Analysis of the team's trajectory

The scientific project for the next contract relies on three axes: 1) genetic link between cancer and chronic inflammation; 2) biomarkers of metastatic disease and blood-brain barrier; 3) cancer therapy using gold nanoparticles targeting resistance to antiangiogenics. One concern is that there is only one permanent Inserm researcher for the next contract (1 DR), so there is a risk of not having sufficient full-time human resources to implement the project and supervise young researchers. In order to support the team leader, the first axis will be co-led by a senior researcher (PUPH position). This axis is identified as high-risk high-gain. A young researcher (PH position) will be involved as a co-leader of the second axis, and a confirmed researcher (IR position with HDR) will co-lead the third axis.

To implement the first research axis, the team will seek new collaborations with mathematicians, especially from future Team 4 (ATIPE Team), which could be a way to partly address the issue, in addition to strengthening the interactions between the different teams in the Unit. A joint grant has also been submitted with Team ATIP-Avenir of the Unit. Other grants have been submitted by the team leader, in particular Plan Cancer 2022, and there are plans to submit to ERC (starting grants and synergy grants).

RECOMMENDATIONS TO THE TEAM

The team is encouraged to pursue its policy of collaborating with the other teams of the unit. It is also encouraged to participate in larger scale collaborative projects from national and/or international funding agencies, preferably as a coordinator but also as a partner. This could help hire post-docs and attract young researchers who would be able to lead the different research axes in the long term, so that the research can be pursued even without the close supervision of the team leader.

Efforts to engage in international (EU-level, bi-national) projects is highly recommended to increase funding opportunities. Moreover, active recruitment of international PhD and Post-Doc level students would be highly advantageous and to increase the impact of published work.

CONDUCT OF THE INTERVIEWS

Date(s)

Start: 12 octobre 2023 à 8 h

End : 12 octobre 2023 à 17 h

Interview conducted : online

INTERVIEW SCHEDULE

8:30 a.m. Presentation of committee

8:45 a.m.-9:30 a.m. Highlights of the Unit by the Director (20min presentation+ 20min questions)

9:30 a.m.-9:50 a.m. Team 1: Bio-cibles des dysfonctions cardiovasculaires : Ms Ferial Azibani (10 min présentation : 10 min questions)

9 h 50-10 h 10 Digital Twins for perioperative medicine: Mr Etienne Gayat (10 min présentation : 10 min questions)

10 h 10-10 h 30 Team 2: Bio-cibles de la maladie métastatique en oncologie : Mr Guilhem Bousquet (10 min présentation : 10 min questions)

Coffee break: 15 mn

10 h 45-11 h 45. Committee debriefing

11 h 45 - 12 h 15

Inserm IT Marie Josephe Leroy Zamia

Université Paris Cité : Doyen Faculté santé : Pr Matthieu Resche-Rigon Michel Vidal Doyen UFR médecine : Philippe Ruzniewski et Christine Guillard — Directrice du pôle Recherche et Innovation de la faculté de santé :

Université Sorbonne Paris Nord : Pascale Molinier :

12 h 15-13 H 00 LUNCH

13 h-13 h 30 Meeting with technicians and administrative staff (closed doors)

1:30 p.m.-2 p.m. Meeting with PhD and post-doc (closed doors)

2 p.m.-2:30 p.m. Meeting with researchers not team leaders

Coffee break: 15 mn

2:30 p.m.-3:15 p.m. Closed-door meeting of the committee

3:15 p.m.-3:45 p.m. Meeting with the Directors (present and future)

3:45 p.m.-4:30 p.m. Committee meeting (closed doors)

GENERAL OBSERVATIONS OF THE SUPERVISORS

Le Président

Paris, le 16 janvier 2024

HCERES
2 rue Albert Einstein
75013 Paris

Objet : Rapport d'évaluation de l'unité DER-PUR250024187 - MASCOT - Marqueurs cardiovasculaires en situation de stress

Madame, Monsieur

L'Université Paris Cité (UPCité) a pris connaissance du rapport d'évaluation de l'Unité de Recherche MASCOT – Marqueurs cardiovasculaires en situation de stress

Ce rapport a été lu avec attention par la direction de l'unité, dont vous trouverez un courrier en annexe, 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.

Avec le Doyen de la Faculté de Santé, nous remercions le comité pour la qualité de son évaluation. En dehors des remarques factuelles émises par de la direction de l'unité concernant une chaire de professeur junior (cf annexe), nous n'avons pas d'observations d'ordre général à apporter.

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

Présidence

Référence

Pr/DGDRIVE/2023

Affaire suivie par

Christine Debydeal -
DGDRIVE

Adresse

85 boulevard St-Germain
75006 - Paris



Édouard Kaminski



ANNEXE

Dear President of the HCERES Jury

The Director and Mascot members thank the President of the jury, the experts and the HCERES delegate for the quality of the scientific evaluation and of the discussions with the unit's leaders and member representatives.

We strongly appreciated the positive comments as well as the precise analysis of our weaknesses.

We are grateful that the experts have taken into account the efforts made during the last 5 years to meet the concerns previously made. Particularly we are proud to cite the recruitment of 2 CR CN Inserm researchers, 2 MCU/MCF, 1 engineer, 2 assistant-professors and 2 professors .

Of note, the occurrence of the junior professor chair obtained by Mascot lab was not been quoted by the HCERES committee. This position will be opened in 2024 and, will strengthen the research force of future team 1.

We are pleased that the jury appreciated the attractiveness of the unit, the ability to obtain funding particularly by team 1 and the excellent quality of the scientific production.

We are aware of the few weak points to be corrected such as:

- the lack of ally between team1 and team 2 in applying cooperative grants
- the absence of European contract leadership or ANR,
- the lack of parity regarding HDR,
- the low number of doctoral students vs HDR in some groups.

MASCOT will make all what is possible to correct these weaknesses.

The Director, with the help of the Laboratory Council, will develop appropriate strategies to stimulate the teams with the aim of positively responding to the various weaknesses noticed:

- MASCOT will pursue its policy to improve the ratio between full-time researchers and clinicians through the opportunities of mobility and enrollment.
- The Director will ensure increased recruitment of doctoral students and the quality of their supervision in team 2
- The Director will stimulate and suggest, to all researchers, participation in training & workshops to improve applications for European or national funding and improve rate of success
- The Director & team leaders will encourage and support the youngest to be able to publish in high visibility journal of basic science.
- The Director will guide to identify research items to be prioritized with regards to workforces and time line
- The Director will stimulate exchanges between teams 1 and 2 and, as recommended by the committee, will invite the team leaders to rely even more on senior researchers.
- During the annual (3-day) lab seminar and other meetings of the entire unit, actions will be taken to further improve cohesion between technical engineers and researchers
- Positive efforts will be made to correct the imbalance between the funding obtained by team 1 and team 2

Finally, the HCERES committee noticed that the unit has grown and has been enriched allowing a very pertinent scientific trajectory leading to genuine translational research. All members of MASCOT thank the HCERES Committee for this strong support.

Paris, 9th January 2024,

Monsieur Eric Saint-Aman
Directeur du département d'évaluation de la
recherche
Hcéres
2, rue Albert Einstein
75013 PARIS

Villetaneuse, le 19 janvier 2024

Objet : Rapport d'évaluation DER-PUR250024187 - MASCOT - Marqueurs cardiovasculaires en situation de stress

Cher Monsieur,

Nous faisons suite à votre courriel du 15 décembre 2023 par lequel vous nous avez transmis le rapport d'évaluation de l'unité de recherche MASCOT - Marqueurs cardiovasculaires en situation de stress dirigé par le Pr Alexandre Mebazaa.

L'université Paris XIII – Sorbonne Paris Nord n'a pas de remarques complémentaires à adresser concernant le rapport HCERES de l'UMR MASCOT.

Je vous prie de croire, Monsieur le Directeur, en mes sincères salutations.

La vice-présidente de la commission recherche



Pascale Molinier

Marine MADANI

De: CNRS-Hcéres Evaluation unités
Envoyé: mercredi 20 décembre 2023 06:55
À: Coordinatrice des CIC INSERM; Correspondant INSERM; Correspondant 2
INSERM; Correspondant Sorbonne université; Correspondant Université
Sorbonne Paris Nord 13
Cc:
Objet: RE: Hcéres - demande de retour des observations des tutelles sur le rapport
d'évaluation - DER-PUR250024187 - MASCOT - Marqueurs cardiovasculaires en
situation de stress

Madame, Monsieur,

Je vous remercie de nous avoir transmis de ce pré-rapport et prie de bien vouloir noter que le CNRS n'émettra pas de réponse institutionnelle de type « observations de portée générale ».

Je reste à votre disposition pour tout complément d'information.

Bien à vous,

--

Frédéric FRANCOIS-ENDELMONT
CNRS – DAPP
Direction d'appui aux partenariats publics
3 rue Michel-Ange - 75794 Paris Cedex 16
Secrétariat : 01.44.96.41.10
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