TEXT OF THE CALL FOR PROPOSALS "COHORTES-MICROBIOMES"

Research Program "France 2030"

"Food Systems, Microbiomes, and Health (PEPR SAMS)"

CONTEXT AND OBJECTIVES

The "Food Systems, Microbiomes, and Health" (SAMS) research program, jointly led by INRAE and Inserm, is funded as part of the French government's investment plan, "France 2030." Its goal is to provide a better understanding of the microbiome and the interactions between microbiomes, health, and food, and to identify the conditions necessary for establishing sustainable food systems in order to aid in the design and evaluation of public policies, as well as to prevent and treat chronic inflammatory diseases.

Studies on the human microbiome indicate that an alteration in the relationship between humans and their microbiomes is one of the key factors in the onset and persistence of chronic diseases, which have become a major public health issue.

France benefits from dynamic clinical and epidemiological research that enables in-depth clinical, biological, and nutritional phenotyping of a large cohort of subjects and patients. However, financial and technical constraints limit the characterization of associated microbial ecosystems, particularly in terms of their composition, functions, and metabolites—the products of their activities and those of the host.

To address these challenges, the COHORTES-MICROBIOMES Targeted Project (TP) of the PEPR SAMS aims to support analyses that will enable the characterization of human microbiomes or host-microbiome interactions in healthy subjects or well-phenotyped patients participating in clinical studies or included in existing cohorts. To ensure comparability of data generated during the study of the human microbiota, appropriate sample collection procedures and methods must be followed. In this context, a call for proposals will be organized by Inserm on behalf of the PEPR SAMS management as part of the COHORTES-MICROBIOMES TP.

TERMS AND CONDITIONS OF PARTICIPATION

The selected projects will be part of the COHORTES-MICROBIOMES initiative, and project leaders will participate in scientific events and the sharing of information (results and best practices). Ultimately, this initiative will help establish a benchmark for the microbiomes of the French population and enhance the field's international visibility.

Selected projects will receive financial support for the characterization of microbiomes through omics analyses, primarily shotgun metagenomics and metabolomics. Requests for other omics analyses must be justified based on scientific interest and the data already collected. More specifically, the objectives are to leverage available data and biological samples that have already been collected or can be collected quickly to complement and enhance the studies. Projects must align with the priorities of the "microbiomes and health" pillar and the focus areas of the PEPR SAMS, which aim to identify i) associations between environmental factors and the state of the microbiome-host symbiosis, ii) mechanisms of host-microbiome interactions, or iii) biomarkers associated with human microbiome dysfunction, or iv) preventive or therapeutic approaches.

Depending on the study design, project leaders may request funding for metagenomic and/or metabolomic analyses, or even for other omics analyses if warranted (except for studies associated with Le French Gut). To enhance the analyses, a portion of the funding may be allocated: i) to supplement the collection of information on subjects' dietary habits concurrently with the biological samples to be studied, and/or ii) to fund personnel for the analysis and integration of multi-omic and clinical data.

For this call, two participation options will be available: i) General case: apply as an independent cohort for metagenomic and/or metabolomic analyses (selection of 8 to 10 projects); ii) Specific case: apply by partnering with the Le French Gut project for metagenomic analyses of human fecal microbiota (selection of 3 to 4 projects).

If the consortium does not possess or have access to bioinformatics resources, projects could benefit from the computing infrastructures established by national research institutes (equipe@pepr-sams.fr) or by the targeted project of the PEPR SAMS Cloud4SAMS initiative (cloud4sams-contact@groupes.france-bioinformatique.fr). This project will provide project-specific secure sandbox-based analysis environments, ensuring compliance with legal and regulatory requirements for the analysis of microbiome and health data. It will also offer standardized processing and analysis tools for the field, as well as training for users of this infrastructure. Costs for storage space and computing resources must be included in project budgets. The same applies to the recruitment of personnel needed for data analysis. Please note that Cloud4SAMS does not provide analysis services for projects.

FINANCING DETAILS

Amount: maximum €250 000 (including management fees).

Duration: Eligible projects will have a maximum duration of 3 years, including sample collection (if applicable) as well as the technical phases of data processing and analysis.

ELIGIBILITY CRITERIA

The eligibility criteria below must be met to ensure that projects incorporate the use of standard methods and can be completed within a maximum period of 3 years.

i. This call is open only to clinical trials or observational studies with an existing biological sample collection and/or samples to be collected within a timeframe compatible with the total duration of the project.
ii. Eligible clinical trials or observational studies must involve:
    a. the general population;
    b. or patients with chronic diseases (with control cases where applicable).
iii. Microbiome characterization must be based on samples from subjects or patients in existing clinical trials or observational studies (that have obtained or are awaiting regulatory approval). It is possible to propose a project combining samples from multiple studies.
iv. Analyses must be completed within a timeframe compatible with the duration of funding, i.e., within a maximum of 3 years.

In the event that samples need to be collected and/or consent needs to be re-obtained from participants retroactively, a justification of the feasibility of these operations within the allotted timeframe (3 years) must be provided. In particular, the following must be specified: the number of participants who can be reached, the human and technical resources available to recontact participants, the procedure for signing the new consent form, and the protocol section describing the new analyses. Older studies without a CPP number are not eligible.

For studies currently recruiting participants or awaiting regulatory approval, evidence demonstrating the feasibility of recruiting the necessary participants and collecting the relevant samples will be required. For studies awaiting regulatory approval, funding will be contingent upon obtaining such approval by the date the results of the call for proposals are published.

v. Proposed projects must include detailed phenotypic data (biological, clinical, nutritional, lifestyle, etc.) that have been (or will be) collected in conjunction with microbiome characterization.

vi. Eligible analyses will preferably involve shotgun metagenomic (whole-genome sequencing) and/or metabolomic analyses applied to human stool samples or other ecological niches, as well as potentially to fluids, tissues, or organs for which the sequencing method is to be specified. These analyses may involve cross-sectional and/or longitudinal samples. In cases where analyses are planned to characterize the host-microbiota relationship (transcriptomics, metabolomics, etc.), the existence of associated microbiome data or their generation within the scope of this call for projects must be indicated.

Samples will have been (or will be) collected, stored, and processed using standard methods and procedures:

- For metagenomic characterization of the microbiome, DNA collection and extraction protocols must comply with the Standard Operating Procedures of the International Human Microbiome Standards project (SOPs 002, 003, 004, 005 for collection and the SOPs updated by MetaGenoPolis 006, 007) or analogous methods validated by the community (referenced). For more information, please visit the IHMS (https://human-microbiome.org/index.php#SOPS) or MGPS (https://mgps.eu/standard-operating-procedure/) websites.
- For other omics characterizations and methods, a description and justification of their validity must be provided, referencing publications where possible or offering a specific rationale. If a collection of new samples is planned from an existing cohort, consultation regarding the methods used with the leaders of the PREANALYTICS PC of the PEPR SAMS is required (preanalytics@inserm.fr).

Special case of projects associated with the French Gut

- For projects associated with French Gut, the collection, DNA extraction, and metagenomic sequencing of fecal samples will be carried out via the LFG-SAMS platform. These methods follow the IHMS SOPs cited above. The cost of metagenomic sequencing must be included in the submitted project proposal.

- A minimum of 500 cross-sectional samples will be required to be compatible with the high-throughput approach of the LFG-SAMS platform. Projects proposing fewer than 500 samples may be considered if they justify the reduced number (e.g., rare participants or conditions hindering recruitment or collection). The maximum number of samples to be sequenced per project is 2,000. In addition to these cross-sectional samples, a maximum number of longitudinal samples (<20% of total samples) may also be included.

- Projects will benefit from shared support for the bioinformatic analysis of metagenomic and nutritional data, coordinated by the INRAE MetaGenoPolis unit. A justification of internal resources enabling the performance of statistical analyses aimed at cross-referencing microbiome data and metadata will be required. To supplement these resources, financial support for the recruitment of staff dedicated to analysis (interns, postdocs, engineers), for a maximum duration of six months per project, may be budgeted.

- Project leaders are invited to contact the Le French Gut team (Cellexe-FG@inrae.fr) to confirm the feasibility of the collaboration. A letter confirming this feasibility, issued by the sponsor of the Le French Gut study, is required to apply.

- Project leaders must ensure that the study sponsor approves of the project and the collaboration with Le French Gut.

PROCEDURE FOR THE CALL FOR PROPOSALS

First step

This essential and selective stage will determine the project's technical eligibility and scientific relevance, which will be assessed via a questionnaire and a letter of intent respectively.
Letters of intent must briefly describe the project's objectives and the clinical trial(s) or cohort(s) on which they are based. The mandatory questionnaire will enable the committee to assess the eligibility of the proposed study based on the required quality and feasibility criteria.
A panel will be set up by the PEPR SAMS management and may, where appropriate, propose the merging of projects that have been selected.

Second step

This stage will involve a consolidation phase for the projects shortlisted for final selection.
The steering group for the "COHORTES-MICROBIOMES" project will be available to project leaders to answer their questions during the project development phase.
An independent international panel will be set up by the PEPR SAMS management to select the winning projects.

PREVISIONAL SCHEDULE

The provisional schedule is available on the call for proposals page.

DOCUMENTS REQUIS POUR LE DÉPÔT

Online forms (website address for submission): https://www.eva3.inserm.fr/login

CONTACTS

PEPR SAMS management: equipe@pepr-sams.fr

Technical support for the application submission platform: eva.dsi@inserm.fr