Priority Research Programme (Programme Prioritaire de Recherche - PPR) on antibiotic resistance

Call for proposals

"Integrated microbiology and multi-omics data platform"

SUMMARY

The implementation of **an integrated microbiology and multi-omics data platform and the development of digital tools** is envisaged in support of the French Priority Research Programme (Programme Prioritaire de Recherche - PPR) on antibiotic resistance. This national programme is funded by a budget of €40 M as part of the third investment programme for the future (Programme d'investissements d'avenir - PIA3).

This platform, financed by the General Secretariat for Investment (Secrétariat Général pour l'Investissement - SGPI), is one of the four essential tools identified by the antibiotic resistance PPR programme. Its objective is to integrate all disciplines and data on antimicrobial resistance into a "One Health" cross-sectoral approach.

BACKGROUND

The problem of transmission and dissemination of resistance represents a global challenge. All sectors of human (general practice and hospital setting) and veterinary medicine (livestock, aquaculture, domestic and wild animals), as well as the contamination of the environment (soil, water, effluents) by antibiotics, resistant bacteria and resistance genes must be taken into account. Furthermore, the study of antimicrobial resistance must go beyond bacteria, parasites, fungi and viruses responsible for infections, and include all reservoirs (including hosts) contributing to the emergence and spread of resistance in the context of current global changes (climate, biodiversity loss, etc.).

An array of data collection systems and analysis tools have been developed and are available in France. However, these systems are segmented based on their respective objectives and field of operation (e.g. based on fundamental research, clinical data, surveillance, monitoring, etc.), and above all compartmentalised according to sectors focused on humans, livestock (terrestrial or aquatic), environment (soil, aquatic ecosystems, effluents, water treatment, agriculture, atmosphere) or wildlife. Omics approaches (genomics, metagenomics, transcriptomics, proteomics, lipidomics and metabolomics) are essential for a detailed understanding of the processes and mechanisms involved in the selection, transmission and dissemination of antimicrobial resistance.

The interconnection and interoperability of data and associated analytical tools related to antimicrobial resistance, accessible under a common open access portal, would be a considerable asset to increase resources and opportunities for data exploitation, and boost research in a holistic, cross-sectoral approach. The collection of information in the form of metadata, at the molecular, cellular, tissue, organ or organism level and more broadly at the population and community level, are

becoming increasingly varied and complex, requiring new mathematical and computational approaches, including artificial intelligence, to enable their exploitation (from data processing to risk modelling). These data also include those derived from patents or breakthrough technologies.

OBJECTIVES OF THE CALL FOR PROPOSALS

In order to provide essential research tools to combat antimicrobial resistance, it is critical to establish **a dedicated platform of integrated and interoperable multi-omics microbiological databases and develop custom-made bioinformatics tools**. This platform should meet the needs of the scientific communities on both facets (multi-omics and mathematics/bioinformatics) and the tools developed will have to be integrated into the national platform. This resource will provide support and structure to all four research pillars of the antibiotic resistance PPR programme.

The objectives of this call are to respond to current urgent needs:

1. **Host a national multi-omics platform and coordinate the network that will depend on it,**
2. **Create and implement biobanks and integrated multi-omics microbiological databases** for the Human-Animal-Environment sectors, while ensuring the interoperability of these databases with each other and with epidemiological databases. These include in particular, the health data depositories of the French University-Hospitals Centres (CHU), the national health data system and the Health Data Hub. It will also be important to facilitate the exchange of biological materials and samples between laboratories with complementary expertise (traceability systems, integration of historical data, data certification, etc.). These data will be coordinated and hosted by the national platform, and if necessary linked to infrastructures attached to the PIA3.
3. **Develop, in parallel, mathematical and (bio)informatics tool kits** to model the evolution of antibiotic resistance, the transmission and dissemination of clones and genes within and between sectors, and evaluate the impact of global interventions and current global changes.

The biobanks, databases and tools made available through this interconnected platform will allow to:

- Document “sensitivity-resistance” phenotypes, referencing strains of Human-Animal-Environment origin, genes and proteins implicated in bacterial resistance (regulators, repressors, enzymes, transporters, etc.), and data relevant to the study of antibiotic dose-effect (target, structure-activity, etc.)
- examine mechanisms of diffusion of pathogenic bacteria and of emergence of bacterial infectious diseases (human, plant or animal, including zoonosis) taking into account environmental and anthropogenic factors, while integrating the notion of multi-pathologies that could favour the emergence of resistance,
- model parameters of emergence, diffusion, exposure or elimination of antibiotic resistance and contribute to the definition of indicators of the progression of epidemics beneficial for a predictive approach,
- identify populations and geographical regions at risk, and contribute to the preparedness against epidemic or pandemic risks,

- analyse data, including those regarding mechanisms of host-pathogen interactions, immunology, inflammation and immunopathology, in the context of resistance acquisition and escape from treatment, including antibiotic susceptibility.
- measure and evaluate the activity of antimicrobial molecules (screening tools, methods and platforms, and structure vs activity kinetics or dynamics studies) and currently studied or established adjuvants, capable of potentiating antibiotic activity in relation to mechanisms of resistance.

For the development of this platform, the main requirements are to:

- **Build on existing initiatives, tools and teams with relevant (bio)informatics and/or mathematical expertise.** An initial inventory has been made identifying tools (software, annotation, machine learning and modelling), expertise and potential host institutions of the platform. Potential synergies with current infrastructures and EquipEx+ of the PIA3 are of relevance in the context of this inventory.
- **Define and manage strict access, ownership and confidentiality rules** for both databases and tools, which are to be made accessible to the entire scientific community through a common portal.
- **Respond to the need to unify and/or determine formats required for depositing, consulting and exporting data,** especially when it is necessary to federate several teams or laboratories.
- **Define a secure hosting location for the proposed data storage,** either by an existing infrastructure or through the creation of a dedicated facility, including human resources for its development and operations.
- **Implement a harmonised charter of formats and standard operating procedures** validated by different sites and institutions.

FUNDING MODALITIES

In agreement with the directorate of the antimicrobial resistance PPR programme, a budget of €2 million has been assigned by the SGPI for the implementation of an integrated microbiological and multi-omics data platform. This funding is earmarked for the implementation of the three above-mentioned objectives over the course of the next 4 years.

Note regarding the platform: a plan for the financial sustainability of the national platform beyond the first 4 years of funding will have to be anticipated as soon as the platform is implemented. The proposed plan should be in agreement with the supervisory bodies of the institutions involved.

The distribution of the budget according to the objectives is as follows:

- Objective 1 (hosting, data storage, security of data storage and animation of the platform) will be attributed a maximum budget of €400,000.
- Objective 2 (creation, implementation of integrated multi-omics microbiological databases and biobanks) will be allocated a global budget of €1 M distributed over the selected cross-sectoral projects, including equipment and human resources costs.

- Objective 3 (development of mathematical and (bio)informatics tools) will be assigned a maximum budget of €600,000 distributed over the selected cross-sectoral projects, including equipment and human resource costs.

SELECTION CRITERIA

Applicants may respond to the call for proposals by proposing solutions to one or multiple objectives described in the section "Objectives of the call for proposals".

The selection of candidates will be made taking into consideration the components described above.

Prerequisites for the three objectives:

- Belong to a research team affiliated with the public sector,
- Be based in France.

Specific criteria for each objective:

- Objective 1 :
    - Provide a proposal for IT hosting and data protection, IT functionalities and suggested tools, while demonstrating support from the proposed hosting institution,

- Objectives 1, 2 and 3 :
    - Demonstrated experience in the production and processing of omics data, in the establishment, conceptualization or management of omics databases, or in the development of tools for the analysis and/or modelling of omics data,
    - The ability to develop multidisciplinary or multi-partner projects,
    - A multidisciplinary and cross-sectoral vision of the proposed project integrating a "One Health" approach.