



IDI BAPS

Institut
D'Investigacions
Biomèdiques
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TROCAR

Translational Research
On Combating Antimicrobial
Resistance



TROCAR is a project in the LifeSciHealth Priority of the
European Commission Seventh Framework Programme





» The ultimate TROCAR goal is to recommend novel control measures to limit or prevent the spread of highly virulent multi-drug resistant clones. It is an example of modern translational research, from molecule to preventive action.

Concept and project objectives

The driving concept of TROCAR is **to investigate the fundamentals of the epidemiology of new highly virulent multiresistant strains**. The project will focus on: Methicillin-resistant *Staphylococcus aureus* (MRSA); Vancomycin-resistant *Enterococcus* spp. (VRE); Extended-spectrum, metallo- and acquired AmpC beta-lactamase (ESMAC-BL) producing *Enterobacteriaceae*; Multidrug-resistant *Pseudomonas aeruginosa*; and Multidrug-resistant *Acinetobacter baumannii*.

The project will focus on three major strategic aims:

- Definition of the **major high-risk resistant clones** based on an appropriate representative collection and new clinical strains.
- **Genomic and proteomic approaches** to investigating specific traits associated with virulence, transmission, persistence and resistance of epidemic clones in comparison with non-epidemic clones, as well as resistance determinants and their genetic location.
- The development of **bioinformatics tools** to fully exploit the genomics data and allow the rapid identification of resistant strains with heightened epidemic potential.

By combining the outputs of the project it will be possible to provide the scientific basis for an early warning system when isolates of a particular epidemicity appear in the community and in nosocomial settings. TROCAR will create a knowledge base to recommend novel control measures that limit or prevent the spread of highly virulent multi-drug resistant clones. It is an example of modern translational research, from molecule to preventive action.

Moving beyond the state-of-the-art

The dramatic increase of new antibiotic resistance genes and the prevalence of bacteria resistant to multiple antibiotics are reason for concern. The problem includes not only the spread of clonal strains but also of mobile genetic elements.

The existing programmes for surveillance of antimicrobial resistance are mostly observational and lack studies designed to provide scientific understanding of the epidemiology, virulence and resistance mechanisms at the genomic and proteomic levels. Currently, epidemiological methods are not applied in most resistance surveillance studies, therefore far greater epidemiologic rigour is needed to better understand the impact of the resistance.

TROCAR introduces novel elements to control nosocomial and community spreading of highly virulent multi-drug resistant strains of bacterial pathogens. The coherent **genomic and proteomic approach** will provide a more detailed knowledge of the fundamentals of epidemiology, resistance and virulence. Moreover, the **bioinformatics tools** developed will help investigators to analyse the obtained data and design solutions and recommendations for clinical practice.



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Strategic impact



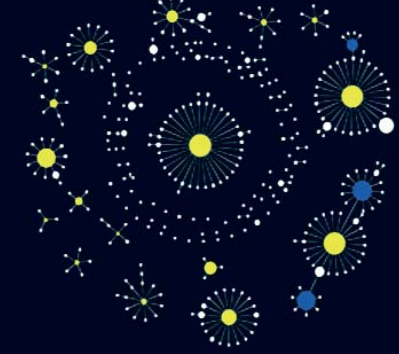
The gap between scientific knowledge and clinical practice in the prevention of dissemination of highly virulent multiresistant pathogens is substantial. Therefore, it is critical that initiatives such as TROCAR are implemented to provide basic biological information about these pathogens.

The ultimate goal of TROCAR is to define genotypic or phenotypic traits of highly virulent multiresistant strains of MRSA, VRE, ESMAC-BL *Enterobacteriaceae*, multidrug-resistant *P. aeruginosa* and *A. baumannii* for the improved design of control strategies. Resistance, transmissibility and virulence are likely interlinked and they can be considered the vertex of a triangle that covers a coherent strategy to control the increase of antimicrobial resistance and dissemination of multiresistant microorganisms.

The project will mobilise experts from around Europe and generate data from many regions. It will then be possible to build up the full picture of the current dissemination of high-risk clones of the aforementioned microorganisms.

» The project will mobilise experts from around Europe to provide basic biological information about paradigmatic pathogens. The results will provide information to create the whole picture of the current dissemination of high-risk clones.

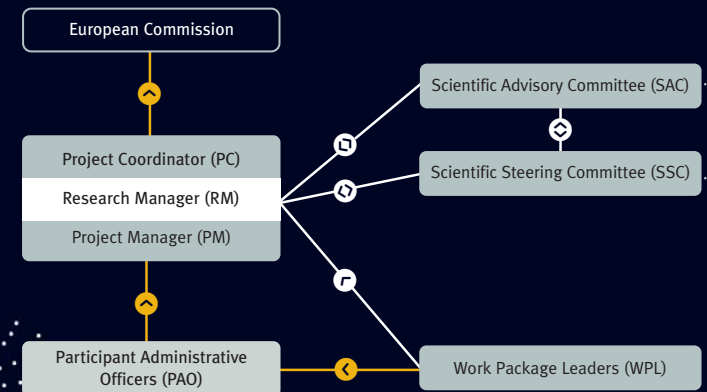
Management structure



The complementarity and broad multidisciplinary nature of the TROCAR consortium has meant that close collaboration is needed to ensure efficient project management. The management and coordination is organised in 3 main components: **Scientific Steering Committee (SSC)**, **Scientific Advisory Committee (SAC)**, and **Management Group (MG)**.

HIGHLIGHTS OF THE TROCAR MANAGEMENT SYSTEM

- Excellence of coordinator
- European capabilities of the consortium
- Quality assurance
- External Scientific Advisory Committee (SAC)
- Knowledge management
- Mobilising partner resources
- Efficient technology transfer



— Administration
— Technical

Workpackages

WP1

PROJECT COORDINATION ACTIVITIES

OBJECTIVES

- Simple and robust management system.
- To ensure and support efficient internal management of TROCAR: efficient communication between the coordination core and the Commission.
- Agreement upon good working practices, project principles and production.
- Adherence to the tolerances and acceptance criteria for each workpackage.
- Delivery of regular financial and progress reports to EC.

DELIVERABLES

- Drafting of the Consortium Agreement.
- Drafting of the interim periodic reports to the Commission.
- Communication tools (leaflet, website, media).
- Drafting of the final periodic reports to the Commission.

WP2

THE EPIDEMIOLOGY AND DATA EXCHANGE PLATFORM

OBJECTIVES

- To establish, maintain and consolidate the coherence of existing European and national network structures of antimicrobial resistance surveillance and reference services.
- To establish the necessary criteria for inclusion of pathogens into the state-of-the-art research line.
- To create an inventory of strains of bacterial pathogens with emerging importance for public health.
- To analyse the geographic abundance and migration patterns of HiRiC.

DELIVERABLES

- Setting up the collaborative TROCAR network of dedicated surveillance laboratories and reference laboratories in Europe.
- Establishing criteria for inclusion of MRSA, VRE, MDR *P. aeruginosa* and *A. baumannii*, and ESMAC-BL producing *Enterobacteriaceae* in the research line.
- Inventory of strains of MRSA, VRE, MDR *P. aeruginosa* and *A. baumannii*, and ESMAC-BL producing *Enterobacteriaceae* with emerging importance for public health, currently co-circulating in European hospitals and communities.
- To make accessible an interactive website based on GoogleMaps or equivalent geographical information system, displaying the geographical abundance and migration patterns of high-risk clones in Europe.

WP3

COMPARATIVE GENOMICS AND PROTEOMICS OF ESTABLISHED AND EMERGING MRSA EPIDEMIC CLONES

OBJECTIVES

- To establish a catalogue of MRSA clones circulating in Europe.
- Comparative genomics of MRSA clones.
- To investigate the phenotypic and genotypic characteristics of the *S. aureus* isolates circulating in Europe.
- Identification of new highly discriminative targets for the rapid differentiation of clones and for intervention.

DELIVERABLES

- Detailed genotypic and phenotypic characterization of representative *S. aureus* isolates circulating in Europe.
- Full-genome sequencing and comparative genomics of six epidemic MRSA clones and identification of twelve potential targets for rapid differentiation of clones.
- Application of automatic annotating tools for genomic data to establish a predicted secretome map of epidemic MRSA strains.

WP4

DECIPHERING VANCOMYCIN-RESISTANT *ENTEROCOCCUS FAECIUM*

OBJECTIVES

- To establish a catalogue of VRE clones circulating in Europe.
- Comparative genomics of VRE clones.
- To analyse the structure and composition of vancomycin resistance plasmids.
- Comparative proteomics of VRE clones.

DELIVERABLES

- Data on dissemination of major VRE clones characterized by genotypic and phenotypic tests in participating European countries.
- Data on genomes of three VRE with different epidemic strength.
- List of differential surface and secreted proteins and virulence factors between epidemic and commensal strains.
- Protocols for molecular tests to detect and discriminate highly-virulent, hospital adapted VRE strain.



WP5	WP6	WP7	WP8
<p>EXTENDED-SPECTRUM, METALLO- AND ACQUIRED AMPC BETA- LACTAMASE (ESMAC-BL) EMERGING THREATS IN ENTEROBACTERIACEAE</p> <p>OBJECTIVES</p> <ul style="list-style-type: none"> • Surveillance data collection on ESMAC-BL in Europe. • Identification of emerging successful clones (HiRiC) and mobile element harbouring ESMAC-BL genes. • Genomics of selected plasmids harbouring ESMAC-BL genes. • Physiology, ecology, and virulence of ESMAC-BL producing organisms. • Rapid detection of ESMAC-BL producing organisms: influence on intervention. <p>DELIVERABLES</p> <ul style="list-style-type: none"> • Collection of HiRiC - ESMAC-BL producing <i>Enterobacteriaceae</i>. • Full sequencing and annotation of plasmids harbouring <i>bla</i>_{ESMAC} genes in epidemic strains or that have disseminated among multiple strains (estimate 6 plasmids). • To identify new physiological and virulence traits contributing to the persistence and dissemination of ESMAC-BL producing organisms and their corresponding genes. • New tools enabling the rapid and simple detection of resistance genes in current and emerging circulating ESMAC-BL producing <i>Enterobacteriaceae</i>. 	<p>GENOMICS, DRUG RESISTANCE AND PHYSIOLOGY OF MDR <i>PSEUDOMONAS AERUGINOSA</i> AND <i>ACINETOBACTER BAUMANNII</i> STRAINS</p> <p>OBJECTIVES</p> <ul style="list-style-type: none"> • To identify representatives of widespread MDR clones. • Analysis of the resistome of the selected strains for resistance determinants. • Investigation of uncommon/still unclear mechanisms for clinically relevant resistance traits. • Comparative genomic analysis of some MDR strains/R-plasmids. • Analysis of virulence traits of MDR <i>A. baumannii</i> strains and interaction with biofilm. <p>DELIVERABLES</p> <ul style="list-style-type: none"> • Definition of a set of strains, from available collections, representative of <i>P. aeruginosa</i> and <i>A. baumannii</i> of clinical significance for physiological investigations. • Resistome of selected MDR <i>P. aeruginosa</i> and <i>A. baumannii</i> strains. • Data on genomes of 4 <i>P. aeruginosa</i> and 4 <i>A. baumannii</i> and sequence analysis of epidemiologically-relevant plasmids (total 4-6 plasmids). • List of specific virulence traits and differential surface and secreted proteins between epidemic and non-epidemic strains. 	<p>COMPUTATIONAL BIOLOGY AND EVOLUTIONARY ANALYSIS</p> <p>OBJECTIVES</p> <ul style="list-style-type: none"> • Establishment of databases. • Complete genome sequencing of bacterial chromosomes. • Multilocus sequence data based on mobile elements. • Complete genome sequencing of mobile elements. <p>DELIVERABLES</p> <ul style="list-style-type: none"> • Establishment of chromosomal MLST databases and population analyses. Development of plasmid MLST schemes. • Scripts in place for the rapid detection and characterization of sequences / novel genes of potential clinical relevance from draft and complete genome sequences. • Analysis of plasmid MLST data, results of phylogenetic comparisons and refinement of models. 	<p>DISSEMINATION AND EXPLOITATION</p> <p>OBJECTIVES</p> <ul style="list-style-type: none"> • Dissemination. • Exploitation results. <p>DELIVERABLES</p> <ul style="list-style-type: none"> • Development of channels for the active dissemination of information. • Annual conferences for the presentation of the results. • Establishment of a platform for companies and their associations as main action of a technology implementation plan (TIP). • Plan for the use and dissemination of foregoing.

The consortium

The consortium of researchers includes many internationally recognised experts whose expertise spans diverse fields, including medical microbiology, genomics and proteomics, molecular typing and population genetics, antimicrobial resistance, bacterial pathogenicity and computational analysis. Moreover, the project is conducted under the patronage of European Society of Clinical Microbiology and Infectious Diseases (ESCMID), the leading scientific society in the field of human infection in Europe.

These research groups will provide a Network of Excellence to fill the knowledge gaps in partnership with a network of national and regional institutes and laboratories that identify imminent health threats to the communities and hospitals in Europe imposed by novel and successful bacterial pathogens.



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For further information:
www.trocarproject.eu

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