

 <p>UniSR Università Vita-Salute San Raffaele</p>	<p>APPLICATION TO ACT AS SUPERVISOR AND RESEARCH PROJECT PROPOSAL</p>	<p>MO 20-5 ed. 01 del 21/02/2025 PO 20 Page 4 of 11</p>
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PROJECT

Supervisor: Andrea Maurizio Cabibbe

Title: Evaluating minimally-invasive sampling and culture-free Next Generation Sequencing-based approaches for the rapid detection of infections and antimicrobial resistance

Curriculum: Clinical and Experimental Medicine

Link to the personal page of the University or relevant hospital site website: <https://research.hsr.it/en/divisions/immunology-transplantation-and-infectious-diseases/emerging-bacterial-pathogens/andrea-maurizio-cabibbo.html>

Description of the Project (max 3,000 characters including spaces)

Background/gap of knowledge

Rapid detection of infections is essential for timely treatment, improved patient outcomes, and effective infection control. Traditional pathogen diagnostic approaches often rely on invasive sampling methods and lengthy culture-based techniques, which can delay decision-making and public health responses. There is a growing need for alternative, minimally invasive sampling methods and advanced pathogen identification and typing technologies. Metagenomics can enable comprehensive pathogen detection, antimicrobial resistance and virulence profiling directly from clinical samples.

Rationale and hypothesis

Minimally-invasive samples, such as exhaled breath or capillary blood, are easier to collect and better suited for scale-up in diverse populations. This project will evaluate their diagnostic potential when analysed using metagenomic short-reads sequencing and/or adaptive sampling for long-reads sequencing and other rapid assays.

We hypothesise that next generation sequencing, including metagenomics, and new rapid molecular tests applied to minimally invasive samples enable faster and comprehensive detection of pathogens and resistance markers, offering a scalable alternative to conventional diagnostic methods for systemic (e.g. sepsis) and local infections.

Objectives and specific aims



The overall objective of this PhD project is to evaluate the diagnostic potential of minimally invasive samples for infections using metagenomic, long-reads NGS, and emerging platforms, with a focus on detecting bacterial and viral pathogens, and antimicrobial resistance in diverse clinical and public health contexts.

Specific Aims

To assess and compare the diagnostic yield of short- and long-reads metagenomic and NGS-based approaches applied to different minimally invasive sample types

To benchmark these technologies against standard microbiological and molecular diagnostics in terms of sensitivity, specificity, and breadth of pathogen detection.

To optimise sample processing workflows and bioinformatics pipelines for low-biomass, minimally-invasive samples.

To explore the application of new molecular tools (e.g. CRISPR-based diagnostics, targeted and whole-genome enrichment) in complementing metagenomic analyses.

Expected outcomes

The PhD project will deliver a comprehensive evaluation of the diagnostic potential of metagenomics and NGS-based methods for detecting transmissible pathogens in minimally-invasive samples like exhaled breath or peripheral and capillary blood. It will demonstrate how these methods compare to standard diagnostics in terms of pathogen detection and AMR profiling. Optimised protocols for low-biomass sample processing, including nucleic acid extraction and bioinformatics pipelines, will be established. The feasibility and scalability of these methods will be confirmed in real-world clinical and field settings. Ultimately, this research has the potential to improve global health by advancing accessible, cost-effective diagnostic tools.

Skills that the student should acquire (max. 600 characters including spaces):

The student will acquire skills in wet NGS techniques, bioinformatics for NGS data analysis, and other molecular biology techniques like nucleic acid extraction and CRISPR-based . The student will develop protocols for low-biomass samples, validate diagnostic methods, and conduct research in clinical and field settings. Skills in statistical analysis, global health applications, and project management will also be essential. Strong communication abilities will be crucial for presenting findings and collaborating with multidisciplinary teams.



References (max. 15)

T. Vos et al., The Lancet, 396 (2020) pp. 1204-22

C. Boehme et al., The Lancet, 9 (2021) pp. E247-E49

C.C. Wang et al., Science, 373 (2021) pp. Eabd9149

Z. Xiaojing et al., ACS sensors, 10.1021 (2025) acssensors.5c00021.

G.A. Goig et al., The Lancet Microbe, 10.1016 (2020) e175-e183

K.N. Govender et al., Microbial Genomics, 10.1099 (2022) mgen.0.000886