

## Development of a point-of-care device for fast detection of pathogens involved in hospital acquired infections

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### Introduction:

Hospital-acquired infections are considered one of the leading causes of death Worldwide. Moreover, according to the Centers of Disease Control and Prevention (CDC), more than 70% of the bacteria now causing hospital-acquired infections are resistant to at least one of the drugs most commonly used to treat them. This is the consequence of the extensive exposure of patients to heavy antibiotic use. In addition to this, Intensive Care Units (ICU) patients have an increased risk of infection due to their underlying diseases or conditions, impaired immunity, and exposure to multiple invasive devices. Among pathogens causing hospital infections, methicillin resistant *Staphylococcus aureus* (MRSA), vancomycin resistant enterococci (VRS) and carbapenem resistant *Acinetobacter baumannii* (CRAB) have become predominantly reported. Problematic of hospital-acquired infections and resistance to antibiotics is due, in part, to the inability to rapidly detect, identify and thus, to treat patients within the early stages of infections and consequently, efforts should be made to make hospitals as safe as possible by preventing such infections.

Lab-on-chip devices are a promising technology for pathogen detection enabling at an increased response speed, sensitivity and portability, presenting the necessary features for point-of-care diagnostics. In these devices, biochips are combined to electronic and microfluidic platforms enabling a multiplex detection signal acquisition and processing. Magnetoresistive (MR) sensors on lab-on-chip platforms have promising characteristics as sensing devices, namely the use of magnetic nanoparticles as reporter systems that can selectively concentrate the target bacteria, reducing the time for enrichment and improving the detection limit. In a standard biochip-based bioassay, the specificity of the biorecognition elements is the most important aspect of biosensor development for pathogen detection to enhance detection of true positives while minimizing the probability of false positives and negatives. Bacteriophages (or phages) are viruses that infect bacteria. They specifically recognize and bind to bacteria and are capable to discriminate between live and dead cells and recognize viable but non-cultivable bacteria (VBNC) bacteria. Moreover, they are cost-effective, robust, thermally and chemically stable and easy to conjugate with other motifs such as biomolecules or nanoparticles offering potential as probes for specific biosensing. Moreover, some of their proteins such as the receptor binding proteins (RBPs) and the cell wall binding domains (CBDs) of phage endolysins are responsible for the phage host recognition and thus are promising molecules to be used as biorecognition elements *per se* on biosensing platforms.

### Aims:

This project aims at developing a fast detection method to be used in hospitals for the identification of pathogens responsible for problematic nosocomial infections, namely methicillin resistant *Staphylococcus aureus* (MRSA), vancomycin resistant enterococci (VRS) and carbapenem resistant *Acinetobacter baumannii* (CRAB). The method will be based on a magnetic capture of the target bacterial cells from biological samples (fluids, swabs..) by using bacteriophages or derives thereof as sensing elements. The detection of the target bacteria will be performed on a magnetoresistive platform followed by the identification of the presence of resistance genes amplified by PCR and detected by spectrophotometry.