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. Among pathogens causing nosocomial infections, methicillin resistant *Staphylococcus aureus* (MRSA), vancomycin resistant enterococci (VRS) and carbapenem resistant *Acinetobacter baumannii* (CRAB) have become predominantly reported. The problematic of hospital-acquired infections and antibiotic resistance is due, in part, to the inability to rapidly detect, identify and thus, to treat patients within the early stages of infections. Point-of-care (POC) devices are a promising technology for pathogen detection enabling an increased response speed, sensitivity and portability. In these devices, biochips are combined to electronic and microfluidic platforms enabling a multiplex detection signal acquisition and processing. Magnetoresistive (MR) sensors have promising characteristics as sensing devices, as they are highly sensitive and allow a discrete quantification of magnetic entities which, when related to the number of molecular recognition events, results in a quantitative analytical mode.
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, sensitive and accurate multiplexed POC device to be used in hospitals for the detection of pathogens responsible for problematic nosocomial infections, namely methicillin resistant S*taphylococcus aureus* (MRSA), vancomycin resistant enterococci (VRS) and carbapenem resistant *Acinetobacter baumannii* (CRAB).
To achieve this goal, the POC will integrate a sample preparation module and a magnetoresistive platform so that biological samples can be directly loaded and analysed. For the detection and quantification of the target bacteria, magnetoresistive (MR) sensors integrated along with microfluidics and associated with magnetic particles as reporter systems will be used. The specificity of the assay will rely on the use of bacteriophages or derives thereof as sensing elements. Additionally, the POC will incorporate an optical system based on gold nanoparticles, enabling the identification of antibiotic resistance genes on the targeted bacteria.
Overall, it is envisaged that the developed POC will allow patient's samples to be screened specifically for nosocomial pathogens and their antibiotic resistance, with sample-in-answer-out results in few hours.