Development of a Lab-on-chip Platform for Diagnosis of Urinary-Tract Infections

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Urinary tract infections (UTIs) are among the most common types of infections in both hospitalized and community patients and thus pose a significant healthcare burden. Around 90% of these infections are caused by bacteria, which have been shown to be increasingly resistant to antibiotics. Complicated UTIs occur mainly in patients with indwelling catheters, but also in those undergoing urological surgery or with debilitating diseases. If not treated in the early stages with adequate antibiotics, UTIs can evolve to chronic pyelonephritis, renal failure or urosepsis, resulting in considerable morbidity and mortality.

The gold standard for the diagnosis of a UTI is the detection of pathogens by using the bacteriological urine culture, which takes 3-7 days and thus is time-consuming and laborious.

Despite there are some diagnosis methods to detect bacteria in urine, there is a lack of a rapid, specific and sensitive method that allows the multiplex detection of bacterial cells and thus can provide a timely antibiotic treatment.

To address this unmet need, this project aims to develop an integrated multiplex lab-on-chip (LoC) device capable of accepting urine samples with the endpoint generation of a signal upon detection of bacterial cells. This will be achieved by synergistically combining the high specificity of bacteriophages as specific probes with the miniaturization and automation of microfluidic devices and the sensitivity of magnetoresistive sensors.

Microfluidics technology offers many advantages for pathogen detection such as automation, high-throughput, miniaturization, small sample volume, portability and rapid detection time. Also, modular devices integrating several functionalities in only one chip have been reported, and currently, most of the lab bench operations can be translated on chip by rationally designing the different device modules.

Microdroplets in microfluidics is the alternative to lab-bench reactions allowing for a fine control and homogeneity over reaction conditions in microisolated environments. Moreover, mixing in droplets have demonstrated to be very efficient, providing a higher control over local concentrations and homogeneity.

Magnetoresistive (MR) sensors associated with magnetic particles as reporter systems have promising characteristics namely response speed, high sensitivity, and simple operation. Moreover, can be integrated along with microfluidics on LoC devices, allowing a confined and simplified signal acquisition and quantification. In order to confer the specificity and selectivity of the biosensor, bacterio(phages), which are natural bacterial viruses, or their proteins, can be promising biorecognition molecules for bacterial detection.

AIM:

On this project, we will combine droplet-based microfluidics, bacteriophages and magnetoresistive sensors to create a lab-on-chip to simultaneously detect and quantify specific bacteria from UTIs. This device will integrate as main functionalities two differentiated modules, one for sample preparation and a second module for detection and quantification. The sample preparation module is based in microdroplets technology to increase the mixing efficiency of the phage-labelled NPs and the bacteria of interest. The detection module will include an array of MR sensors that will detect the fringe field of the magnetic labels (with the bacterial cells) when an external magnetic field is applied. This will allow the detection and quantification of the target pathogens prevalent in UTIs.