# Nanophotonics Biosensors for the clinical management of bacterial infectious diseases

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Infections by pathogenic bacteria and their multidrug resistance have become a major healthcare issue in the XXI Century. Bacterial Infections result in millions of cases every year and in an increasing incidence of deaths. In Europe 5-10% of all hospitalizations results in nosocomial infections, especially in surgical and intensive care units (ICU). This is 4.1 million patients, of which 37,000 die. These infections contribute to serious events including long stays at hospitals, additional antibiotic treatment and susceptibility to further infections, risk of developing sepsis, and the need of advanced medical intervention, resulting in a strong economic and heath impact. The early detection of bacterial infections increases dramatically the chances of survival. The alarming rise of antibiotic-resistant bacteria aggravates this global health concern. The massive use of antibiotics has promoted intense selective pressure on bacteria, contributing to the emergence and spread of the resistant mutants. Common illnesses as pneumonia, postoperative infections, or tuberculosis are becoming increasingly untreatable. According to the Review on Antimicrobial Resistance (AMR-review.org), at least 50,000 lives are lost each year in Europe and US due to infections caused by antimicrobial-resistant bacteria. Moreover, this number is increasing alarmingly year by year and it could become the first cause of death in which 10 million victims per year are envisioned at the horizon 2050.

A critical barrier for managing infections and antibiotic resistance is the lack of rapid diagnostics, resulting in either the use of unnecessarily broad first-line antibiotics, or long delay in administering the appropriate one. TWO pages abstract format: including figures and references.

The use of point-of-care nanophotonics biosensors as rapid diagnostic platforms can fill in the gaps in the problematic situation of the rapid and accurate diagnostics of infections by providing sensitive, reliable, quantifiable and selective analysis, while reducing test and therapeutic turnaround times, decreasing and/or eliminating sample transport, and using low sample volume.

Within the PHITBAC project (www.phitbac.es) we aim to introduce such new, disruptive, and versatile point-of-care nanobiosensor technology for the whole diagnosis and clinical management of bacterial infectious diseases. The groundbreaking diagnostic device will prove rapid detection of most relevant pathogenic bacteria, including an on-site identification of antibiotic resistance, and a personalized monitoring of antimicrobial therapy effectivity.

We have already demonstrated the detection of E. coli at extremely low concentrations (LOD~4 CFU/mL) in human ascitic fluid in a direct format for spontaneous bacterial peritonitis detection, with a time to result of only 25 min and no need of any sample purification. Moreover, we have detected P. aeruginosa (LOD~30 CFU/ML) and methicillinresistant S. aureus (MRSA), both being considered two of the most prevalent bacteria associated with nosocomial infections. Our approach enables the specific identification of the resistant pathogen (MRSA) and its differentiation from methicillin-susceptible S. aureus (MSSA) [1]. Moreover, we have developed an ultrasensitive methodology for the detection of genes associated with the multidrugresistance found in Gram-negative bacteria as E. coli without using any PCR amplification step [2]. We have detected genes encoding several β-lactamase enzymes able to hydrolyze a broad spectrum of beta-lactams. As a proof-of-concept, we detected two genes of the unamplified genomic DNA directly extracted from bacteria commonly found in samples of patients attended at Vall d'Hebron Hospital. All the steps took 30 min, achieving an estimated LOD of only 28 aM (~10e5 copies) [22], one of the most sensitive DNA detection without amplification or labelling steps reported up to date.

## References

[1] J. Maldonado, M.-C. Estévez, A. Fernández Gavela, J.J. González-López, A.B. González-Guerrero and L.M. Lechuga. Analyst 145 (2020) 497

[2] J. Maldonado, A.B. González-Guerrero, A. Fernández-Gavela, J.J. González-López and L.M. Lechuga, Diagnostics 10 (10), (2020) 845