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Cleavable Peptides for the detection of bacterial organisms in biological systems

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Anti-microbial resistance (AMR) is an ongoing, growing global threat in which infectious microorganisms, such as bacterial and fungal cells, have developing an innate immunity towards conventional medicine treatment. Because of that, it has led to the development of highly infectious organisms that will be difficult to provide subsequent treatment in the future. The World Health Organization (WH) has listed the rise of antimicrobial resistance organisms as one of their key priorities, where it was estimated that in 2019, AMR was associated with nearly five million deaths globally; and by 2050, it was further estimated that more than US $1 trillion will be spent on AMR-linked patient treatment.

One of the major factors that has led to the rise of AMR is due to current medical practices and treatment. Surprisingly, most AMR microorganisms are acquired within a healthcare environment. Hospital-associated infections (HAIs) are the leading cause for the development of newly resistant microorganisms. Within this setting, either: i) patients are emitted under the suspicion of having an infection, or ii) acquire an infection while under care. In either case, patients are provided treatment to manage their symptoms, where it common practice for doctors and clinicians to prescribe a wide range of different and generic medications. Unfortunately, due to these actions, the use of different and generic medications has led to a variety of microorganisms to slowly develop an innate immune against these drugs.

One method to reduce the rise of AMR and subsequent HAIs is to minimise the misuse and overuse of medicines for treatment infections. For healthcare providers to prescribe the ideal medication and dosage, analytic and diagnostic tools are needed to correctly identify the pathogen and assess the severity of the infection. However, current diagnostic tools are either too slow or not specific to identify the pathogen in a timely manner. Cleavable peptides have emerged as a promising recognition site as they can be engineered for high specificity and selectivity towards the targeted analyte. Therefore, for this work, we have developed a fluorescently labelled peptide sequence that can be used to detect the presence of *Pseudomonas Aeruginosa* without the need of sample preparation. By further conjugating the peptide onto a fluorescently labelled nanoparticle, a Förster resonance energy transfer (FRET) event can occur, leading to the development of an ultra-sensitive diagnostic tool. Therefore, for this presentation, we will be discussing the development of this nanosensor for *Pseudomonas Aeruginosa* detection.

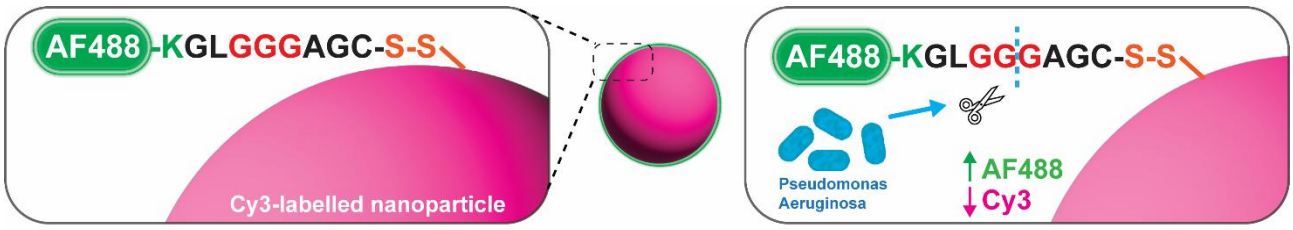

Figure 1: Schematic of the fluorescently labelled nanoparticle-peptide biosensor (nanosensor). Here, a cyanine3 (Cy3) labelled nanoparticle were used as a scaffold to attach our modified peptide sequence. Because of the sequence length, the two fluorophores create a FRET effect, where Alexa Fluor 488 is quenched. In the presence of *Pseudomonas Aeruginosa,* the peptide sequence is cleaved, allowing for the fluorescence of AF488 to recover, allowing for the development of a highly sensitive biosensor.

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