New TURN-ON probes for the detection of bacteria in body fluids

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Résumé

Due to the spread of antibiotic-resistant pathogens, bacterial infectious diseases became one of the first causes of mortality and morbidity in the world1,2. Early administration of an appropriate antibiotic considerably reduces the risk of mortality3. However, the current methods of clinical detection and identification of bacteria in body fluids (urine, blood...) are insensitive and time-consuming due to the bacterial culture step. In our team, we aim at developing rapid and direct next-generation methods for clinical diagnostics of bacterial infections using fluorescent probes.
We have conceived a family of environmentally sensitive fluorescent probes for bacteria by conjugating a fluorogenic and solvatochromic dye Nile Red to antimicrobial peptides (AMP) and antibiotics targeting different components of the bacterial cell envelope. The probes were characterized by excellent fluorescence turn-on between aqueous and apolar media, and a positive solvatochromism similar to those of the parent dye. Applied to the analysis of bacteria by radiometric flow cytometry, these probes should allow the analysis of the difference in the microenvironment of the components of the cell envelope.4

With the goal to increase the fluorogenic character of the Nile Red-derived probes and to reduce their non-specific fluorescence in the presence of serum, we developed a family of bacteria-targeting probes based on aggregation-caused quenching (ACQ)5. The probes are composed of a peptide backbone to which are attached covalent dimers of Nile Red. In an aqueous medium, the dimeric probes exist in the form of non-fluorescent π-stacked H-aggregates, whereas in an apolar medium (bacterial cell membrane), the fluorescence is restored, leading to a strong fluorescence turn-on. Moreover, the strong interaction between the two fluorophores prevented dimer dissociation in the presence of serum, thereby opening up prospects for the application of Nile Red-based dimers in body fluids.

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Mots-Clés: fluorescent probes, fluorogenic detection, Nile Red, bacterial detection