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Differentiating RNA from DNA by a molecular fluorescent probe based on the "Door-Bolt" mechanism Biomaterials

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ABSTRACT: Although excellent florescent probes have been developed for DNA, good probes for RNA remain lacking. The shortage of reported and commercial RNA probes is attributable to their severe interference from DNA. As DNA and RNA have similar structures but different functions, it has been an imperative challenge to develop RNA probes that differentiate from DNA. In this study, an NIR fluorescent probe, **NBE**, is described, which contains a bulky julolidine group that can fit in a spacious RNA pocket and emit intense fluorescence. However, **NBE** has no response to DNA, as it cannot intercalate into the double strands or even in the DNA minor groove. The sensing mechanism is similar to the effect of a door-bolt. **NBE** shows excellent performance in RNA sensing (outstanding photostability, high selectivity and fast response), whether in aqueous buffers, fixed cells or living cells. These findings might provide not only a potential imaging tool but also a new design strategy for the recognition of RNA while avoiding interference from DNA.

Introduction

Since being discovered in 1868,[1] ribonucleic acid (RNA), which is generally composed of four building blocks, adenine, cytosine, guanine and uracil, has attracted considerable interest due its vital roles in biological processes. Among other functions, RNA is well-known to perform active roles in the coding, regulation, and expression of genes.[2, 3] For the past several years, the important roles that RNA play have been recognized not only in viruses (RNA is the core genetic material of HIV)[4] and bacteria (certain RNAs act as enzymes)[5] but also in mammals[6] besides humans[7][8].

Acquiring the complete spatial-temporal profiles of RNA synthesis, transport, and processing is critical to understanding cell function and behavior in conditions of disease, health, and external stimuli. Accordingly, considerable effort has been devoted to the development of probes for imaging RNA in living cells. Although numerous oligonucleotide RNA probes, such as molecular beacons, have been extensively studied, RNA-selective fluorescent stains with low molecular weight, membrane permeability and fast response are more convenient and have attracted increasing attention.

To date, although many excellent DNA fluorescent probes have been developed,[9-27] probes for RNA are rare.[28-32] The only commercial RNA staining dye is a green dye, known as “SYTO RNA-Select”. The shortage of RNA probes is due to interference from DNA. Recently, several RNA probes were reported[33-44]. These investigations demonstrated that interference from DNA is still an intrinsic obstacle to overcome for RNA detection and imaging.