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Optical aptasensors for quantitative detection of small biomolecules: A review

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ABSTRACT

Aptasensors are aptamer-based biosensors with excellent recognition capability towards a wide range of targets. Specially, there have been ever-growing interests in the development of aptasensors for the detection of small molecules. This phenomenon is contributed to two reasons. On one hand, small biomolecules play an important role in living organisms with many kinds of biological function, such as antiarrhythmic effect and vasodilator activity of adenosine. On the other hand, the concentration of small molecules can be an indicator for disease diagnosis, for example, the concentration of ATP is closely associated with cell injury and cell viability. As a potential analysis tool in the construction of aptasensors, optical analysis has attracted much more interest of researchers due to its high sensitivity, quick response and simple operation. Besides, it promises the promotion of aptasensors in performance toward a new level. Review the development of optical aptasensors for small biomolecules will give readers an overall understanding of its progress and provide some theoretical guidelines for its future development. Hence, we give a mini-review on the advance of optical aptasensors for small biomolecules. This review focuses on recent achievements in the design of various optical aptasensors for small biomolecules, containing fluorescence aptasensors, colorimetric aptasensors, chemiluminescence aptasensors and other optical aptasensors.

Contents

Abbreviations: EIAs, enzyme immunoassays; ELISAs, enzyme-linked immunosorbent assays; FRET, fluorescence resonance energy transfer; MB, molecular beacon; PNK, polynucleotide kinase; CAMB, catalytic and molecular beacon; ssDNA, single-stranded DNA; dsDNA, double-stranded DNA; EB, ethidium bromide; AP site, apurinic/apyrimidinic site; ATMND, 2-amino-56,7-trimethyl-1,8-naphthyridine; AgNCs, Ag nanoclusters; CuNPs, Cu nanoparticles; MG, Malachite green; AuNPs, Gold nanoparticles; NMM, N-methyl mesoporphyrin IX; SPR, surface plasmon resonance; HRP-mimicking DNAzyme, horseradish peroxidase-mimicking DNAzyme; ABTS, 2,2-azino-bis(3-ethylbenzothiazoline-6-sulfonicacid) diammonium salt; TMB, 3,3,5,5-tetramethylbenzidine sulfate; CL, chemiluminescence; TMPG, 3,4,5-trimethoxyl-phenylglyoxal; CRET, chemiluminescence resonance energy transfer; ICIA, indirect competitive inhibition assay; AuNRs, gold nanorods; SERS, surface-enhanced Raman scattering; RS, resonance scattering; DLS, dynamic light scattering

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1. Introduction

Biosensors are devices that transform the recognition of targets into a physically detectable signal, such as optical, electronic mass or magnetic signal. Generally, a biosensor contains two essentially functional components: target recognition and signal transduction. Theoretically, recognition component is the key for the sensor performance. An ideal recognition component should possess these characteristics of high sensitivity, admirable selectivity, fast response, robust performance and versatility for various targets. With these criteria, antibody and aptamer are two of the mostly used recognition component. Antibodies, responding to specific antigens, have been widely applied in the construction of various sensors. Enzyme immunoassays (EIAs) and enzyme-linked immunosorbent assays (ELISAs) are two of the most common methods. However, as a functional protein, antibody is sensitive to circumstance and its activity is unstable. What is more, it is difficult to obtain antibodies for molecules too small and molecules with high toxicity or poor immunogenicity, which limits its widespread application (Liu et al., 2009).

Alternative, aptamer is single-stranded oligonucleotide with impressive recognition feature. As a strong rival to antibody, aptamer has high affinity and selectivity. The high affinity is attributed to the remarkable dissociation constants (K_d) ranging from picomolar to nanomolar levels between aptamer and its target (Brody et al., 1999). The excellent selectivity is stemmed from the reason that aptamer can distinguish even minor structural differences between targets and their analogs (Jenison et al., 1994). In addition, aptamers possess many other competitive advantages over antibody. Firstly, aptamers can bind with a broader range of targets, including metal ions, amino acids, other small organic molecules, viral proteins, even cells and bacteria (Ueyama et al., 2002; Harada and Frankel, 1995; Stojanovic et al., 2000; Koch et al., 2004; Bruno and Kiel, 1999; Wang et al., 2003). Secondly, aptamer can be successfully obtained from synthetic chemicals with the characteristics: higher purity and lower costs. Thirdly, aptamers can be flexibly modified with various chemical tags including fluorescence probes, electrochemical indicators and nanoparticles. They can also be modified with enzymes to minimize their degradation. Finally, aptamers are small in molecular weight and superior in stability, which can bear repetitious denaturation and renaturation. Overall, these unique characteristics make aptamers an ideal recognition element for biosensors.

As to the signal transduction, electrochemical, optical, mass-sensitive transduction modes have been applied to biosensors (Cheng et al., 2009; Zuo et al., 2009; Zhou et al., 2010; Wen et al., 2011; Ruan et al., 2012; Shu et al., 2013; Liu et al., 2013; Huang et al., 2013; Kobu et al., 2013; Lim et al., 2010; Lu et al., 2011; Zeng et al., 2012; Fu et al., 2013; Iliuk et al., 2011). Among them, optical analysis has been widely developed because of high sensitivity, quick response and simple operation. Coupling aptamer as the recognition component with various optical analytical techniques as the signal transductions, optical aptasensor provides special opportunities for the analysis of targets.

Up to now, numerous optical aptasensors have been developed for the detection of small molecules, proteins and metal ions (Zeng et al., 2012; Zhang et al., 2013; Liu et al., 2009). Specially, the quantitative detection of small biomolecules increasingly attracts much more interest of researchers due to its important physiological function. The normal amount of small biomolecule is crucial for organisms, while the amount too high or too low will cause certain diseases. For example, adenosine, an endogenous nucleoside, has potent antiarrhythmic effect and vasodilator activity. Its content also affects the peripheral and central nervous system (Wu et al., 2007). ATP, as energy currency in cells, is essential in living organisms. Its concentration is an important indicator for disease diagnosis such as cell injury and cell viability (Zeng et al., 2012). Therefore, the quantitative detection of small biomolecules is important in biomedical, diagnosis and treatment of diseases (Kerman et al., 2006; Shankaran et al., 2007; Chughtai and Heeren, 2010).

To date, many optical aptasensors for various small biomolecules have been developed, such as ATP, adenosine, cocaine, dopamine, NAD^+, ochratoxin A, theophylline, flavin mononucleotide, tyrosinamide, kanamycin, oxytetracycline, glucose, bisphenol A (Li et al., 2012, 2013; Ye et al., 2013; Song et al., 2012; Fu et al., 2013; Zhou et al., 2011a, 2011b; Zheng et al., 2011; Lu et al., 2011; C. Yang et al., 2011; X.H. Yang et al., 2011; Galarreta et al., 2013; F. Li et al., 2009; M.J. Li et al., 2009; Chávez et al., 2010; Stojanovic and Kolpashchikov, 2004; Guieu et al., 2011; Song et al., 2011; Kim et al., 2010; Wang et al., 2013; Lee et al., 2011). All these analytes are listed in Table 1. Nevertheless, there are still few reviews focused on this field (Famulok, 1999; Walter et al., 2012). Moreover, they are mainly focused on the recognition of aptamer with its targets. A review on the development of these optical aptasensors for small biomolecules will give readers an overall understanding of its progress and provide some theoretical guidelines for its future development. Hence, we give a mini-review on the advance of optical aptasensors for small biomolecules, with emphasis not only on the recognition between aptamers and its targets but also on the design of signal transduction. In the following context, we will summarize these recent advances in optical aptasensors for the quantitative detection of small biomolecules. The context can be broadly divided into four categories: fluorescence aptasensors, colorimetric aptasensors, chemiluminescence aptasensors and other optical aptasensors.

2. Fluorescence aptasensors

Fluorescence is one of the most common optical techniques and has been widely applied to aptasensors because of its unique