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Review

Nanomaterial-assisted aptamers for optical sensing

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ABSTRACT

Aptamers are single-strand DNA or RNA selected *in vitro* that bind specifically with a broad range of targets from metal ions, organic molecules, to proteins, cells and microorganisms. As an emerging class of recognition elements, aptamers offer remarkable convenience in the design and modification of their structures, which has motivated them to generate a great variety of aptamer sensors (aptasensors) that exhibit high sensitivity as well as specificity. On the other hand, the development of nanoscience and nanotechnology has generated nanomaterials with novel properties compared with their counterparts in macroscale. By integrating their strengths of both fields, recently, versatile aptamers coupling with novel nanomaterials for designing nanomaterial-assisted aptasensors (NAAs) make the combinations universal strategies for sensitive optical sensing. NAAs have been considered as an excellent sensing platform and found wide applications in analytical community. In this review, we summarize recent advances in the development of various optical NAAs, employing various detection techniques including colorimetry, fluorometry, surface-enhanced Raman scattering (SERS), magnetic resonance imaging (MRI) and surface plasmon resonance (SPR).

Contents

1. Introduction

Aptamers are short single-strand DNAs (ssDNAs)/RNAs that bind diverse targets beyond DNAs or RNAs with high affinity and specificity, which are normally screened with a combinatorial

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technique called systematic evolution of ligands by exponential enrichment (SELEX). In the process of SELEX, more than 10^{10} number of random sequences of nucleic acids in the initial libraries are subjected to a selection pressure, resulting in an exposure of sequences with binding properties. The ssDNAs/RNAs binding to the target are then eluted from the mixture. After polymerase chain reaction (PCR) amplification, the products are subjected to the next round of selection. The selection cycles continue until the final high-affinity ssDNA/RNA species for the target are identified. It is believed that nucleic acids not only play crucial roles in biological processes, but also are versatile tools for target recognition in analytical community. Since discovery in 1990s (Tuerk and Gold, 1990; Ellington and Szostak, 1990), many aptamers have been selected for corresponding targets including metal ions, organic molecules, biomolecules, and even microorganisms/cells, relying on their special three-dimensional (3D) structures. When aptamers bind their targets, they may either incorporate small molecules into their nucleic acid structures or be integrated into the structures of macromolecules (Hermann and Patel, 2000). In comparison with their equivalents of antibodies, aptamers possess several advantages for construction of biosensors such as cost-effective synthesis, high binding affinities for their targets (Brody et al., 1999) and flexibility for signal transduction and detection (Liu et al., 2009). Moreover, aptamers are superior to antibodies in bioanalysis owing to the lack of immunogenicity (Nimjee et al., 2005) and stability against biodegradation and denaturation (Liu and Lu, 2006). Finally, it is easy to design diverse ultra-selective probes for specific targets based on the well-known secondary structures of aptamers with minimum knowledge of their tertiary structures (Liu and Lu, 2004, 2007a).

It is well-known that a sensor consists of at least two elements, namely, target recognition and signal transduction. Once high-specificity aptamers are attained, the next advancement in aptamer sensors (aptasensors) would be employment of novel strategies for sensitive biosensing. Nanomaterials have recently emerged as ideal candidates enabling efficient signal transduction and amplification in aptasensors. The nanomaterial-assisted aptasensors (NAAs) display unprecedented advantages in sensing applications and have attracted significant interests of multidisciplinary study. Since several previous reviews have covered principles and applications of aptasensors (Hamula et al., 2006; Song et al., 2008; Liu et al., 2009; Nguyen et al., 2009), we herein focused on the design and working performance of optical NAAs where the optical detections are adopted for aptasensor signal harvesting. These optical NAAs can be analyzed in-depth as followings:

The NAAs are sensing platform with high selectivity and sensitivity. Generally, aptamers change their conformation after binding with targets. By taking advantage of the conformation change, it allows designing reasonable sensing platforms with assistance of nanomaterials. The selectivity of a sensing approach is achieved by capitalizing on the binding affinity and specificity of aptamer to its target, while the sensitivity is dependent on the capacity of nanomaterials to transduce the binding event to detectable signal.

The optical NAAs are to transduce aptamer recognition events to physically measurable signals. Optical detection methods such as colorimetry, fluorescence, surface-enhanced Raman scattering (SERS) and surface plasmon resonance (SPR) are most widely adopted for signal harvesting in aptasensors because of their ease of use and high sensitivity. Also, fluorescence, SERS and magnetic resonance imaging (MRI), are suitable for *in vivo* sensing, showing great potential for practical applications. Nanomaterials in NAAs usually magnify the transduced originally weak signals by several orders of magnitude in aptasensors, which make the optical NAAs highly sensitive.

In this review, for good understanding of optical NAAs, the highlights and prominent examples were summarized, based on various detection methods such as colorimetry, fluorometry, SERS, MRI and SPR. The latest advances and prospects in the development of NAAs were also discussed.

2. Approaches to bioconjugate aptamers with nanomaterials

In NAAs, aptamers and nanomaterials usually work as labels for supporting each other, dramatically broadening the extension of biological applications. For optimization of NAAs, it is important to verify the combination methods of aptamers and nanomaterials. Nanomaterials exhibiting unique surface effect provide facile ways for interacting with aptamers. Mainly, there are two bioconjugation approaches for coupling aptamers with nanomaterials, namely covalent linkage and non-covalent linkage. Covalent linking involves a chemisorption method that is widely used. For example, thiolated-aptamers can be easily chemisorbed onto the surfaces of gold nanoparticles (AuNPs) while the amine-labeled aptamers can be easily adsorbed on the surface of carboxyl-modified silica nanoparticles (SiNPs). Non-covalent assembly involving a physical adsorption provides an alternative bioconjugation approach. Li and Rothberg (2004a,b) found that negatively charged aptamer can adsorb onto negatively charged AuNP surface based on electrostatic adsorption mechanism. This finding has assisted to create modification-free bioconjugations and opened possibility for simple, time-saving analysis procedure. Based on complementary electrostatic interactions, polyamine with positive charge in solution can act as a bridge between aptamer and nanoparticle and promote the weak surface adsorption (Graham and Faulds, 2008). Specific biomacromolecular interactions such as streptavidin/biotin complementarity have also been applied to provide aptamer–nanomaterial binding. For instance, streptavidin-coated nanomaterials would easily adsorb biotinylated aptamers onto their surface. The hybridization of aptamers and nanoparticle-tagged DNA has also been used to conduct NAAs for target detection, which is another popular format for combining aptamers with nanomaterials (Zhao et al., 2007a). The above mentioned approaches are expected to conduct integrated NAA sensing systems and to enhance the recognition efficacy and transduced signals.

3. Applications of NAAs for optical sensing

3.1. Colorimetric assay

Metallic nanoparticles possessing size-/distance-dependent optical properties are ideal candidates for colorimetric assays. For example, the color of colloidal gold is sensitive to its aggregation/dispersion due to varying interparticle plasmon coupling and resulting surface plasmon band shift. Furthermore, owing to AuNPs' extinction coefficient being over 1000 times higher than that of organic dyes (Ghosh and Pal, 2007), the AuNP-based colorimetric recognitions provide considerable sensitivity (Rex et al., 2006). Accordingly, assembly/disassembly of nanoparticles can be considered as the novel indicator of colorimetric assay. AuNP-based colorimetric sensing has been a subject of great interest over the past decade, which takes advantage of the color change that results from the interparticle plasmon coupling during AuNPs aggregation (red to purple/blue) or redispersion of AuNP aggregates (purple to red). Since invented for DNA analysis (Mirkin et al., 1996), the colorimetric assay has been expanded for the detection of a variety of targets, including proteins (Pavlov et al., 2004; Huang et al., 2005), metal ions (Liu and Lu, 2003), small organic compounds (Zhao et al., 2008) and even whole cells (Medley et al., 2008).