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Guest Editor's Introduction

Editorial for "Recent advances in DNA-based biosensor"

DNA has emerged as a versatile molecule for the development of biosensors due to its ability to recognize not only complementary nucleic acids, but also metal ions, small molecules, proteins and cells. Seminal studies in the 1990s led to the discovery of nucleic acid aptamers [1,2] that are capable of binding to specific ligands with affinities rivaling those of protein enzymes and antibodies. Furthermore, a range of functional nanomaterials such as graphene oxide (GO), carbon nanotubes, and gold nanoparticles (AuNPs) have been identified to interact with DNA [3]. These exciting discoveries have paved the way for the development of an extraordinary number and diversity of DNA-based biosensors for the determination of biologically and environmentally relevant analytes [4]. The twenty diverse chapters that follow in this special issue of Methods provide a current snapshot of recent developments in the field of DNA-based biosensors. We hope that by showcasing a range of different strategies from researchers around the world, the reader will gain an insight into the cutting-edge advancements that are taking place in this field, as well as develop an appreciation of the strengths (and limitations) of current technologies.

The G-quadruplex is a non-canonical DNA secondary structure that has been widely used as a signal transducing element in sensing applications. This issue begins with a comprehensive review by Sintim and co-workers [5] highlighting the application of G-quadruplexes as detection or enzymatic labels for the detection of nucleic acids. This is followed by an article from Kong that discusses the factors that are important in determining the performance of G-quadruplex DNAzyme-based sensors, including the nature of the DNA sequence, the components of the solution, the reaction substrates, and an enrichment strategy for G-quadruplex DNAzymes [6]. The next four articles describe the application of luminescent transition iridium(III) complexes for DNA-based sensing applications. Ma, Leung and co-workers employed a G-quadruplex-specific luminescent iridium(III) complex and a guanine-rich oligonucleotide/cupric ion (Cu^{2+}) ensemble as a recognition unit for the analysis of histidine [7]. A parallel G-quadruplex–selective iridium(III) complex has also been developed for Ca^{2+} ion detection in aqueous solution [8]. Furthermore, assay methods for biologically important enzyme activities such as 3′ to 5′ exonuclease [9] and polymerase proofreading [10] using G-quadruplex–selective iridium(III) complexes are presented.

The specific detection of DNA and RNA sequences has attracted widespread efforts aimed at rapid genetic profiling and disease diagnosis. Barthelmebs and co-workers review recent advances in two types of DNA-based biosensors, namely genosensors and aptasensors, and discuss current ideas pertaining to the biorecognition element, DNA immobilization strategies and sensing formats [11]. Marquette and co-workers highlight the characteristics of DNA biosensor/biochip platforms for multiplex blood group genotyping [12]. Lin, Li and co-workers present a technique that couples one-step reverse transcriptase polymerase chain reaction (RT-PCR) with microchip electrophoresis (MCE) for analyzing the BCR-ABL fusion gene, which aims to reduce contamination risk and sample consumption compared to conventional RT-PCR [13]. Zhao and co-workers illustrate a novel approach for the ultra-sensitive detection of point mutations by combination of a modified block PCR and endonuclease IV-based signal amplification system. The method could effectively identify mutant target sequences immersed in a large background of wild-type sequences with abundance down to 0.005% [14]. Xing, Zhou, and co-workers developed a sensitive colorimetric detection assay for *Listeria monocytogenes* by combining a hyperbranching rolling circle amplification (HRCA) technique with AuNPs [15]. Lai and co-workers compared the sensor performance of the stem-loop probe (SLP) and linear probe (LP) electrochemical DNA sensors when interrogated using alternating current voltammetry (ACV), cyclic voltammetry (CV), and differential pulse voltammetry (DPV), with the conclusion that the SLP sensor showed an optimal sensor response over a wide range of experimental conditions [16]. Two microRNA (miRNA)-themed techniques are also presented in this issue. Fan, Liu and co-worker report a DNA nanostructure-based electrochemical microRNA biosensor, and describe a protocol for the use of this methodology for the ultrasensitive detection of miRNA [17]. Palatnik and co-workers present an approach termed SPARE (specific parallel amplification of 5′ RNA ends) that performs genome-wide analysis of miRNA processing intermediates [18].

The next four articles describe the application of functional materials in DNA-based sensing. First, Liu and co-workers highlight recent developments in DNA-functionalized hydrogel biosensors for the visual detection of analytes, and also present detailed methods for immobilizing DNA biosensors in monolithic polyacrylamide gels and gel microparticles [19]. Second, Nie and co-workers have developed a novel DNA-templated click chemistry strategy for the homogenous fluorescent detection of Cu^{2+} ions based on click ligation-dependent DNA structure-switching and the selective quenching ability of a GO nanosheet [20]. Taking advantage of the luminescent response of ruthenium(II) complexes and GO upon analyte binding, Shi, Yao and co-workers have successfully realized the detection of cations and biomolecules by employing two complementary strategies: ruthenium(II) complexes acting as the quencher of GO luminescence or GO acting as the quencher of ruthenium(II) complex luminescence [21]. Finally, Leung and

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co-workers report novel nanoparticle-DNA-polymer composites for hepatocellular carcinoma cell labeling, sensing, and magnetic resonance imaging [22]. The authors also provide comparative studies and protocols for the preparation of ultrasmall superparamagnetic iron oxide nanoparticles, circular plasmid DNA and branched polyethylenimine composites for sensing applications.

The remaining two contributions cover two other aspects of DNA-based sensing. Le, Zhang and co-workers illustrate a binding-induced DNA assembly (BINDA) strategy that is able to couple the target-binding event to an amplifiable DNA assembly, and applied solid phase BINDA for the detection of yoctomolar concentrations of proteins [23]. Li and co-workers constructed a sensitive detection system for measuring DNA-protein interactions at a single plasmonic metal nanoparticle level by localized scattering plasmon resonance (LSPR) spectroscopy. In this system, DNA molecules were conjugated to AuNPs through gold–thiol chemistry, and the resulting complexes functioned as single-particle probes of human topoisomerase I [24].

In summary, this issue showcases the creative methods, strategies and applications that have been devised by researchers worldwide in the development of DNA-based biosensors for a variety of analytes. Based on the exciting examples presented in this issue, we anticipate this field would continue to thrive and mature in the years to come. We would like to deeply thank the contributors to this issue of Methods for sharing their knowledge and insight, as well as the reviewers who spent their time in carefully and anonymously reviewing the twenty articles in this issue. Finally, we thank the Editor, Prof. Jean-Louis Mergny, for inviting us to edit this collection, and the journal manager, Mr. Don Prince, for his helpful assistance in preparing the issue.

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