Asian Journal of Chemistry; Vol. 24, No. 1 (2012), 1-6

ASIAN JOURNAL OF CHEMISTRY

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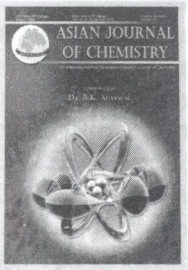

REVIEW

Aptamers as Recognition Elements for Analysis of Small Molecules

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(*Received*: 23 November 2010; *Accepted*: 3 September 2011) AJC-10358

Aptamers, which are functional oligonucleotides selected from random-sequence nucleic acids libraries *in vitro*, possess high recognition ability to specific targets. Owing to their inherent selectivity, affinity and multifarious advantages over the traditional recognition elements, aptamers can be considered as a valid alternative to antibodies or other biomimetic receptors and have been widely employed to design novel analytical methods. In this review, the evolving use of aptamers in analysis of small molecules by exploiting their molecular recognition properties is discussed.

Key Words: Aptamer, Small molecules, Biosensor, Analysis.

INTRODUCTION

For the highly sensitive analysis of small molecules, the selectivity of the recognition element is vital. As a new class of recognition elements, nucleic acid aptamers can recognize a large variety of small ligands, such as amino acids[1,2], nucleotides and derivatives[3,4], antibiotics[5-7] and other small inorganic/organic molecules[8-13]. Aptamers fold upon associating with their ligands into molecular architectures in which the ligand becomes an intrinsic part of the nucleic acid structure. Because the evolutionary pressure on aptamer sequences during selection is directed primarily toward the binding of the ligands, the three-dimensional structures of aptamer complexes reflect highly optimized scaffolds for specific ligand recognition[14]. Therefore, aptamers have high specificity and affinity for their ligands, which highlight the huge potential of aptamers for analytical applications.

Properties of aptamers: The term aptamer is derived from the Latin word "aptus" (meaning 'to fit') and the Greek word "meros" meaning particle[15]. Aptamers are typically single-stranded nucleic acids between 30 and 70 nucleotides in length. They are generated by a process called SELEX (systematic evolution of ligands by exponential enrichment, Fig. 1) which was first reported in 1990[15,16]. SELEX comprises an iterative process of *in vitro* selections using nucleic acid to target binding and partitioning events of unbound nucleic acids in order to isolate high-affinity nucleic acids from large pools of randomized sequence libraries. Starting libraries for SELEX usually contain more than 10^{15} different sequences. The initial library of random-sequence oligonucleotides, which is obtained through combinatorial chemical synthesis, is incubated with a target of interest. Oligonucleotides showing affinity for the target are partitioned by different methods, such as affinity chromatography[10,17], magnetic bead[18], capillary electrophoresis[19,20], microfluidics[21] and so on and then amplified by PCR (for DNA libraries) or reverse transcription PCR (for RNA libraries) to create a new pool enriched in those oligonucleotides having a higher affinity for the target. As this cycle of selection and amplification is repeated, the abundance of the high-affinity oligonucleotides increases exponentially. Negative selection and counter selection are often employed in order to remove aptamers which bind to supports and molecules similar to the target, respectively. Typically after 8 to 15 cycles, cloning and sequencing of the enriched library are carried out, revealing the sequence of oligonucleotides highly specific to the target. Once the sequence information has been obtained, the desired aptamer can be readily produced by chemical synthesis.

The multiple advantages of aptamers include their high specificity and affinity, their easy and highly reliable production by enzymatic or chemical synthesis, their regenerability by simple means and their storability. In addition, advantages over monoclonal antibodies are the higher inhibitory potential and the wider range of chemical modification possibilities because they can be synthesized enzymatically and chemically. Aptamers