Chapter

Introductory Chapter: Oligonucleotides – Overview and Applications

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1. Introduction

Oligonucleotides are polymers of nucleic acids which are building blocks of life. It is one of the key elements of the central dogma of life. Any nucleotide consists of a pentose sugar (ribose in case of RNA and de-oxy ribose for DNA), a phosphate group and any one nitrogenous base (nine-member double ring bases adenine, guanine as purines and six-membered single ring base thymine, uracil and cytosine as pyrimidines). On basis of structure and stability, researchers are working to expand the genetic alphabets [1]. This will extend the diversity of the oligonucleotides and demystification of mystical doctrine like "RNA world hypothesis" [2].

2. Applications

2.1 Oligo-based therapeutics

Oligonucleotides have several applications from encoding, transmitting and expressing genetic information to storage of information, disease diagnostics and even oligonucleotide-based therapeutics. As DNA, RNA is omnipresent in our body, due to its non-immunogenicity, and it also easily be exploited as cargo for drug delivery at specific locations of cellular organelles.

Among whole proteome of our body, only 10–14% of proteins have active binding sites which are "druggable" [3]. To address this issue, nucleic acid-based strategies can exploit translational machinery of the mammalian cells. Antisense oligonucleotides (ASOs) like short single-stranded DNA, phosphorothioate DNA, siRNAs, micro RNAs and locked nucleic acids are key players in drug development processes. There is plethora of ASO-based drugs approved by FDA against several diseases like Duchenne Muscular Dystrophy (DMD), viral diseases, Type2 diabetes, cancer and others. However, poor cellular uptake and rapid degradation or renal filtration DNA-based therapeutics needs modification of delivery module to facilitate internalization and retain their active form [4].

2.2 Oligo-based sensing methods

Besides the carrier of genetic information, breakthroughs in DNA-based biotechniques, CRISPR-based gene editing and other tools revolutionized the nucleotide-based

sensing platforms. Among these sensing techniques, PCR, RT-PCR, antisense technology, single nucleotide polymorphisms in cancer and other deadly genetic disorders played an important role and often been converted into convenient biosensors. In the current COVID pandemic era, DNA-based POC diagnostics played a critical role in early and rapid detection of viral infections and followed to better patient management [5]. Even, to combat the urgent medical emergencies against SARS-CoV2, synthetic DNA-based vaccine was a lifesaver in the process of vaccine development. These nucleotide-based vaccines are amenable to scale-up, cheaper, cold-chain free stable, which are of critical attributes for delivery to resource-limited spaces.

Oligonucleotides having specific target binding or catalytic functions are termed as "Functional DNA". Such an example of functional DNA is "Aptamers", also called "Magic bullets" are considered to be chemical equivalent of monoclonal antibodies for their specificity and sensitivity to their cognate targets [6]. The target repertoire is diverse ranging from small molecules, metabolites, to proteins, cell surface receptors, cells and tissues and even whole organisms. Another major variant of functional DNA is ribozymes or deoxy ribozymes which are analogues of enzymes having specific recognition sites and cleavage activity. They also catalyze certain biochemical reactions. Due to stability, specificity, and variability for the base-pairing hybridization for detection and diagnosis, oligonucleotide-based biosensors are the key shareholder in clinical diagnosis, genome mutation detection and environmental pollutant detection [7, 8].

Recent developments in DNA nanotechnology include advent of various modified functional DNAs (XNAs), DNA computing, logic gates, DNA-based signal amplification strategy which further extended the applications of DNA-based sensors in POC detection, live cell imaging and monitoring, disease prognosis and overall, in health management systems [9].

This book presents a collection of new developments in modified oligonucleotides, cutting edge theranostic applications of oligonucleotides which provide insights and comprehensive overview of this exciting topic to the scientific community.

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