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DNA as a Versatile Building-Block for Bioanalytical and Therapeutic Applications

Kelong Wang*

Department of Chemistry, University of North Carolina, Chapel Hill, NC 27599, USA

Deoxyribonucleic acid (DNA) as the genetic material of the living organisms has been extensively exploited since past decades. In recent years, chemists have begun to engineer DNA for bioanalytical and therapeutic applications. In bioanalytical application, molecular beacons and aptamers are widely used. Molecular beacons are hairpin-shaped oligonucleotides that contain both fluorophore and quencher moieties. They are normally in a turned-off state when the fluorophore and the quencher are brought together; when loop of the molecular beacon hybridize to a nucleic acid strand containing a target sequence they undergo a conformational change that separates the fluorophore and quencher, and in consequence fluorescence is turned "on." Please see review [1] for more details on molecular beacons. Aptamers are single-stranded DNAs or RNAs that have high affinity to their target molecules. Aptamers are selected via a process called Systematic Evolution of Ligands by Exponential Enrichment (SELEX) [2,3]. Application of DNA aptamers in analytical and biomedical sciences was well summarized in the review of You et al. [4]. Molecular beacons and DNA aptamers have been widely used in chemistry, biology, and medical sciences for biomolecular recognition.

DNA can be used in therapeutics by targeting critical disease pathways or carrying therapeutic reagents. With the high affinity and specificity to corresponding proteins or cell surface receptors, aptamers can be used for therapeutic purposes in much the same way as monoclonal antibodies [5]. However, we will discuss more about engineering DNA in delivery of therapeutic reagents because its' characters of biocompatibility, easy synthesis and modification.

DNA aptamer for drug delivery has been achieved by forming hydrogels, micelles liposomes. The Tan group has demonstrated the aptamer–based micelle as drug delivery tool with specificity to bind with target cancer cells [6]. The Tan group has also reported a self-assembled bifunctional unit for selective drug delivery. This platform incorporates a DNA aptamer for cancer cell recognition and a G-quadruplex for drug loading. The modified DNA selectively delivered a photosensitizer 5,10,15,20-tetrakis-(1-methyl-4-pyridyl)-21H,23H-porphine (TMPyP4) to cancer cells; irradiation with visible light generated high toxicity to the target cells [7].

Controlled drug release helps to achieve more effective therapies while eliminating the potential over or under dosing. A variety of control mechanisms have been explored on drug delivery platform. The Bein group has developed a temperature-controlled valve system permitting the targeted release of guest fluorescein molecules from the pores of colloidal mesoporous silica particles [8]. In this work, biotinlabeled DNA double strands were attached to the pore mouths of the core–shell mesoporous nanoparticles. This platform allows a subsequent closing of the pores by the binding of avidin with biotin. The DNA strand melting at the specific melting temperature of the oligonucleotide controls the opening of the valve.

The main concern of DNA based drug delivery platforms is the biostability. In general, wild-type DNA molecules are too susceptible to nuclease-mediated degradation to be useful for most therapeutic applications. To address this, chemically modified non-natural nucleotides and other derivatives have been adopted in engineering DNA and showed enhanced stability against nuclease. Besides the elongation of DNA life time *in vivo*, two more directions are worth efforts of researchers in the future:

1. DNA–based multifunctional platform. The traditional drug delivery may cause side effects, for example a side effect of the doxorubicin liposomal treatment, hand–foot syndrome, is caused by the drug leaking out of capillaries in the hand and feet. DNA aptamers as targeting molecules can be conjugated with drug carrier to alleviate the side effects. In addition, DNA aptamers may also be used with other functional components such as imaging reagents for diagnosis.

2. Controlled release platform, especially a feedback controlled release of therapeutic agent. Because of the complementary binding of the base pairs, DNAs are perfect molecules to construct "on" or "off" switch, or logic gate [9], or feedback loop. With a DNA based feedback loop on the drug delivery platform, releasing dose and speed of therapeutic agent will be well regulated, and this will definitely contribute to the disease treatment.

DNA based bioanalytical and therapeutic methods were mainly the proof–of–concepts in the past decades. We expect that addressing the short comings of DNA stability, the availability of versatile DNA aptamers for different targets will promote more widely usage of DNA in bioanalytisis and therapy.

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***Corresponding author:** Kelong Wang, Department of Chemistry, University of North Carolina, Chapel Hill, NC 27599, USA, E-mail: kelongw@email.unc.edu

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