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Prospects of nanoparticle–DNA binding and its implications in medical biotechnology

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ABSTRACT

Bio-nanotechnology is a new interdisciplinary R&D area that integrates engineering and physical science with biology through the development of multifunctional devices and systems, focusing biology inspired processes or their applications, in particular in medical biotechnology. DNA based nanotechnology, in many ways, has been one of the most intensively studied fields in recent years that involves the use and the creation of bio-inspired materials and their technologies for highly selective biosensing, nanoarchitecture engineering and nanoelectronics. Increasing researches have been offered to a fundamental understanding how the interactions between the nanoparticles and DNA molecules could alter DNA molecular structure and its biochemical activities. This minor review describes the mechanisms of the nanoparticle–DNA binding and molecular interactions. We present recent discoveries and research progresses how the nanoparticle–DNA binding could vary DNA molecular structure, DNA detection, and gene therapy. We report a few case studies associated with the application of the nanoparticle–DNA binding devices in medical detection and biotechnology. The potential impacts of the nanoparticles via DNA binding on toxicity of the microorganisms are briefly discussed. The nanoparticle–DNA interactions and their impact on molecular and microbial functionalities have only drown attention in recent a few years. The information presented in this review can provide useful references for further studies on biomedical science and technology.

1. Introduction

Bio-nanotechnology is a new interdisciplinary field of research and development of nanotechnology with biological, biochemical, or medical applications and activities. It integrates engineering, physical sciences and molecular engineering with biology, chemistry and biotechnology to develop novel devices, such as biosensors, nanomedicines, and bio-photonics, using bio-mimetically inspired nanofabrication techniques. Many nanoparticle-based devices have been developed to meet the requirement of clinical diagnostics for analysis of biological materials. Nanoparticles effectively bridge the biotechnology to provide an access to medical technology, and hold considerable promise of advances in pharmaceuticals and healthcare.

Nanoparticles have received a great research interest in recent decades due to their extraordinary functional properties and increasing applications in manufacturing industry and biomedical technology. Recent advance in nanoparticle technology has encouraged the development of molecular diagnostics, which offer significant advantages over conventional diagnostic systems in terms of sensitivity, selectivity, and practicality in bioassays for DNA and protein markers. The nanoparticles are also chosen as desirable carriers of DNA in target delivery, in order to overcome the drawback of using liposomes due to their inherent problems, such as low encapsulation, rapid leakage in blood, and poor storage stability. The employment of nanoparticles to deliver plasmid DNA, small interfering RNA (siRNA), or antisense oligonucleotides can also waive the unpredictable immune response caused by viral vectors. Nanoparticles are, therefore, expected to play a key role in medical science and technology in the coming decades. The development toward application of nanoparticle based technology in medicines and medical biotechnology continues to be an important research component in medical practice, and will inspire the innovations in this field.

A number of novel technologies based on nanoparticle–DNA binding and their interactions have been developed and used in molecular diagnosis, gene therapy and sensing. These approaches offer an opportunity for the development of efficient and low-cost technologies for disease diagnosis and DNA detection with high sensitivity. All these show that nanoparticle–DNA binding based techniques could have a promising implication in medical biotechnology in near future. In addition to the knowledge of chemical and structural properties (biocompatibility, water solubility, and biodegradability), the fundamentals of energetically favorable molecular binding reactions between

Abbreviations: AFM, atomic force microscopy; Ag-NP, silver nanoparticles; Au-NP, gold nanoparticles; C_{60}, buckminsterfullerene; CHO, Chinese hamster ovary; CNP, carbon nanoparticles; ds-DNA, double-stranded DNA; MWCNTs, multi-walled carbon nanotubes; PCR, polymerase chain reaction; PNA, peptide nucleic acids (PNA); TEM, transmission electron microscopy; SERS, surface enhanced Raman Spectroscopy; SNP, single nucleotide polymorphism; SPR, surface plasmon resonance; ss-DNA, single-stranded DNA; SWCNTs, single-walled carbon nanotubes.

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nanoparticles and DNA is of great importance. It is necessary to understand the interactions within cellular membranes or compartmental molecules. The DNA–nanoparticle interactions through their molecular bindings and biochemical reactions have drawn an increasing interest in recent studies. To our knowledge, there is no specific review paper in this field which is found in the literature.

This minor review will discuss fundamentals of nanoparticle–DNA binding and its associated molecular interaction mechanisms. We only focus on the most commonly used gold, silver and carbon nanoparticles, and highlight their applications for medical biotechnology, in particular for molecular recognition. We present recent discoveries and research progresses how the nanoparticle–DNA binding could vary DNA molecular structure and its bioactivities. We report a few case studies associated with application of the nanoparticle–DNA binding devices in biomedical detection and gene delivery technology. Finally, the potential impacts of the nanoparticles on toxicity of the nanoparticles-contaminated microorganisms are briefly discussed. Integration of these multidisciplinary fields has recently created a new research filed of bionanotechnology, which is expected to have an increasing potential impact on the development of advanced technologies in the future.

2. Mechanisms of DNA–nanoparticle binding

DNA has been a focus of many studies involving nanotechnology. A nanoparticle-based methodology is developed towards applications of sensitive and specific diagnostics, and effective gene delivery systems. High sensitivity can be achieved by one-to-one interactions between a single DNA molecule and nanoparticles through a specific or non-specific molecular binding. DNA can be covalently tethered to the surface of nanoparticles through anchor groups, such as –SH, –OH, $–NH_2$, or –COOH. Gold nanoparticle (Au-NP) or silver nanoparticle (Ag-NP) is usually functionalized with thiolated oligonucleotides, generating DNA–nanoparticle probes for specific DNA hybridization and recognition of complementary sequences of interest.

The non-specific binding between DNA and nanoparticles can be achieved by simple adsorption via non-covalent interactions. Non-covalent binding affinity, similar to those of repressor protein-DNA interactions *in vivo*, is required to control the release of nucleic acids in gene therapy or regulation. Thus, an understanding of such molecular binding reactions at the atomic level is crucial in order to describe the structural and functional basis for the underlying mechanisms. Li and Rothberg (2004a) found that the short single-stranded DNA (24-mer ss-DNA) binds to 13 nm Au-NP and prevents salt-induced aggregation (Fig. 1). However, complementary hybridized oligomers fail to stabilize unmodified Au-NP and result in particle aggregation in saline mixture. It was proposed that these molecular binding reactions can be useful for testing DNA mutation and single nucleotide polymorphism (SNP).

2.1. DNA–gold nanoparticle binding

The selectivity of Au-NP for ss-DNA binding may arise for several reasons. Many researchers believe that electrostatic forces between the anionic DNA strands and the negatively charged surfaces of citrate-stabilized Au-NP are less favorable for double-stranded DNA (ds-DNA) binding. The ds-DNA with higher surface charge density exhibits more repulsion than that of ss-DNA (Gaylord et al., 2002). Moreover, the study on binding affinity of deoxynucleosides to Au-NP revealed that the four deoxynucleosides display high affinities, while the thymine interacts much more weakly with the gold surface than other nucleobases (Storhoff et al., 2002). The duplex DNA structure prevents the exposure of the bases to gold surfaces and therefore limits the DNA–Au-NP interactions (Boon et al., 2000). Finally, ss-DNA is flexible and favors the wrapping around Au-NP, while ds-DNA is relatively rigid and not favorable for wrapping around the Au-NP. The DNA structure may play an important role in DNA–

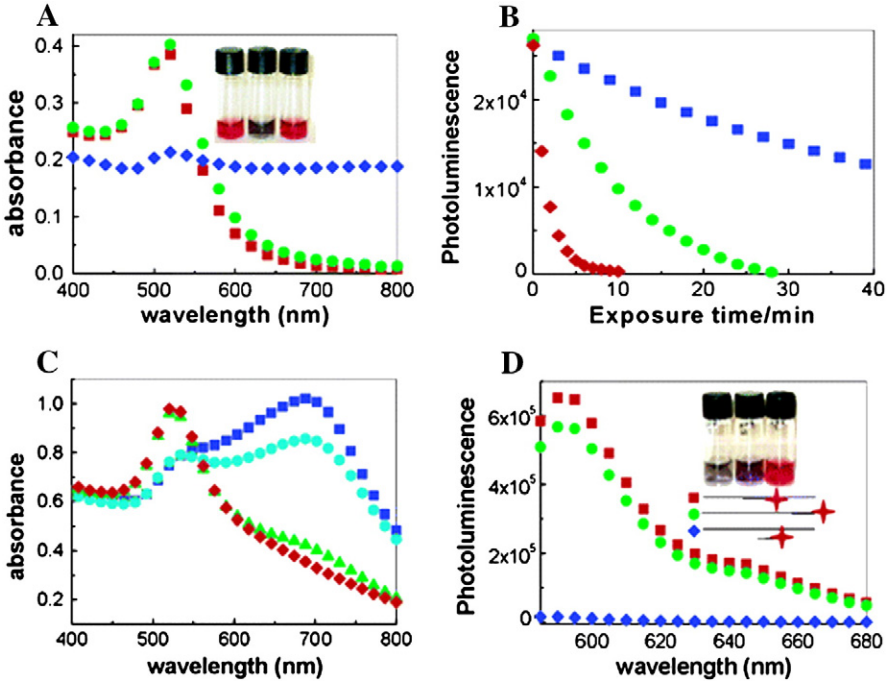

Fig. 1. Adsorption of ss-DNA to Au-NP. (A) Absorption spectra of Au-NP (red), gold nanoparticle with PBS (blue), gold nanoparticle with 24-base ss-DNA first, then PBS (green). (B) Photoluminescence intensity versus time following the addition of rhodamine red-tagged ss-DNAs to Au-NP. 10 mer (red), 24 mer (green), and 50 mer (blue).(C) Absorption spectra of the mixture of ss-DNA (50 mer) and Au-NP heated at different temperature for 2 min, followed by the addition of PBS (0.2 M NaCl). 22 °C (blue), 45 °C (cyan), 70 °C (green), and 95 °C (red). (D) The fluorescence spectra of the hybridized solutions of 15 mer ss-DNA and 50 mer ss-DNA and gold colloid, the 15 mer binding to the 50 mer in the middle (red), at the end (green) and not at all (blue) (Li and Rothberg, 2004a).