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Mini Review

Development of DNA Nanotechnology for Cancer Therapy

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Abstract

Cancer is one of the main causes of worldwide mortality, due to the absence of precise diagnostic tools for the cancer early stages. Thus, early diagnosis, which supplies important information for therapy of cancer timely, is of great prominence for propagation of cancer cells, controlling the growth of the disease, and improving of patients survival rates. To attain the goals of early diagnosis and cancer therapy timely, nanotechnology of DNA can be effective, since it has protruded as a suitable technique for the fabrication of different nanoscale devices and structures. The eventual DNA-based nanoscale devices and structures show wonderful performance in diagnosis of cancer, owing to their small sizes, structures, high programmability and biocompatibility. In particular, the quick development of DNA nanotechnologies, like molecular association technologies, confers DNA-based nanomaterials with more intellectualization and functionalization. In DNA nanotechnology, Watson-Crick DNA molecules are arranged into variety of nanostructures in the range of 10-100nm size under special physical conditions due to electrostatic attraction between free electrons of base nitrogen and phosphate oxygen and sugar. Here, i summarize recent advances made in the development of DNA nanotechnology for the fabrication of intelligent and functional nanomaterials and highlight the potentials of this technology in diagnosis and therapy of cancer

Keywords: Nanomedicine; Nanotechnology; Cancer; Tumor cells; Drug delivery; DNA; Origami

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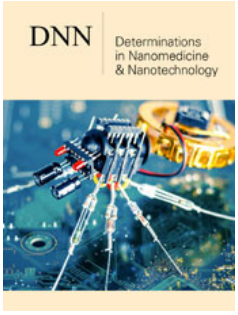

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Introduction

Cancer, a major and increasing worldwide health problem, has already become the second leading cause of death in recent years. As a prime, yet unmet threaten to healthcare globally, cancer gives rise to around 9 million deaths each year in the whole world [1,2]. In order to increase the rate survival of cancer patients, timely therapy and early diagnosis become highly substantial to improve the prognosis of cancer patients, particularly patients who have breast cancer. Drug delivery of molecules specifically to the tumor site is an exigent demand to avoid side effects during therapy of cancer.

The foundation for nano-medicine paths were pioneered by the earlier discoveries:

A. Controlled release system of macromolecules.

B. Liposomes in drug delivery and in transfection of DNA [3].

C. Revolving stealth polymeric nanoparticles [4].

D. Quantum dot bio-conjugate system [5] and

E. Nanowire nano-sensor dates [6].

In addition, for therapy of cancer, researchers have been improving anti-cancer drug delivery systems to target tissues or tumor cells more precisely and produce less side effects compared with chemotherapy [7]. In order to conquer the challenges aforementioned, DNA has drawn a lot of interest, owing to its predictable small size, secondary structure, high programmability, and biocompatibility [8]. Moreover, DNA nanotechnology, a technique applying the biomolecular self-assembly property of DNA, has a broad range of implementations in different disciplines, especially in drug delivery, synthetic biology, and chemical analysis [9].

As a portentous diagnostic and therapeutic nanoplatform, DNA strands combined with other nano materials, such as nanosheets, nanotubes, nanowires, gold nanoparticles (AuNPs), polymers, iron oxides, and quantum dots show a great potential in timely therapy and early diagnosis of cancer [10,11]. This review summarizes modern progress in the development of DNA nanotechnology as shown in Figure 1 and deals with the application of nanotechnology of DNA in intelligent nanomaterials and synthesizing functional for diagnosis and therapy of cancer.

Figure 1: Schematic illustration of different applications associated with DNA nanotechnology.

Preceding Nanostructures of DNA

The chemical and physical properties of DNA nanostructures are registered in excellent published reviews [12-14]. Here, we describe the main elements that are beneficial to understand the self-assembled nanostructure of DNA as nanocarriers drug. The purine and pyrimidine bases that form the nucleotides in single-stranded DNA are attached to pentose sugar and this latter associated unit is known by a nucleoside, which is connected to another nucleoside by the phosphodiester bond. The asymmetric ends of DNA strands are called the '3 and 5' ends depending on whether the terminal group is a free hydroxyl group or a phosphate group respectively. The purine bases are categorized into two types: Guanine (G) and Adenine (A). They have a structure derived from the fusion of six- and five- membered heterocyclic structure, while the pyrimidines are Cytosine (C) and Thymine (T) are six-membered ring (Figure 2A).

In B-form dsDNA, the most prevalent form of double helix, two nucleotide nanowires are twisted around each other with a replicate unit every 3.4nm while maintaining a distance of 3.4Å between the successive base pairs in a double helix with a diameter of 2nm (Figure 2B,2C).

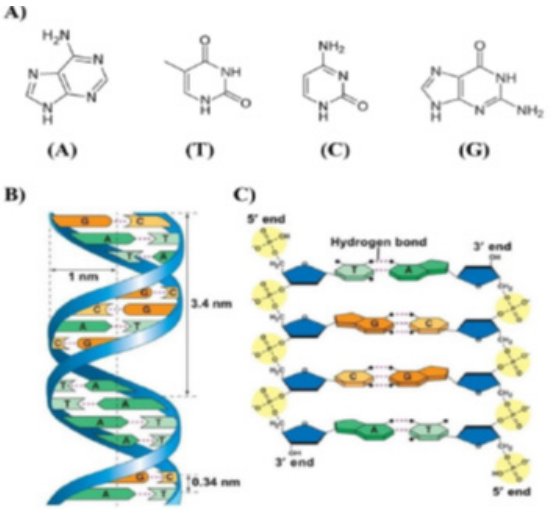

Figure 2: A. Adenine (A), Thymine (T), Cytosine (C) and Guanine (G) of DNA responsible for the robust complementary base pair interactions between DNA strands.

B. Key features of DNA structures.

C. Chemical structure of DNA stabilized by hydrogen bonds between the bases A-T and G-C.

DNA Origami-Based Theranostic Nanoplatform

Nanotechnology of DNA uses the molecular confession properties of DNA to create artificial structures of DNA for technological purposes. DNA origami, a self-assembled structure, is capable of localizing hybridization reactions of DNA on three-dimensional (3D) self-assembled nanostructures or two-dimensional (2D) lattices. Origami nanostructure of DNA is regarded considered as a nanoplatform that can give chances to develop a large number of applications, including drug delivery for cancer therapy and biosensing for cancer diagnosis [15-17]. DNA tetrahedron, a 3D self-assembled DNA origami nanostructure, is widely used as a sensitive biosensing probe which can be rapidly internalized by a caveolin-dependent pathway. Moreover, DNA origami-based molecular recognition elements can be incorporated with anti-cancer drugs to display exerts therapeutic effects on cancer and specific location information of cancer cells at the same time. Doxorubicin hydrochloride (Dox) is well recognized as an operative anti-cancer drug due to its ability of intercalating into C-G base pairs and strong affinity toward double helix of DNA [18,19], so it is widely used as cancer agent.

DNA-Based Drug Delivery

Several DNA-based nanostructures, namely icosahedral, tetrahedral [20], nanotube [21,22], triangle and square have been developed recently for in vitro and in vivo drug delivery applications. In contrast to dsDNA, nanostructures of DNA could be internalized within the cells without any support from transfection agents [23] and, when densely tinned could be effectively used for the drug delivery objectives [24]. The cellular localization of DNA origami could be discovered by fluorescence-based assays, which have the disadvantage of employing fluorescent labels. As alternate path, Okholm et al. [25] use Quantitative real time Polymerase Chain Reaction (QPCR) of M13 amplicons to quantify the cellular absorption of origami structures of DNA [25]. In order to improve and enhance the cell transfection/cellular uptake of DNA-based systems, Mikkilä et al. [26] elucidated the possibility of coating DNA origami via virus capsid proteins, which can self-assemble and bind on the surface of origami through electrostatic interactions and bundle the DNA nanostructures inside the capsid [26]. More recently Brglez et al. [27] designed an intercalator based on acridine derivatives that increased the cell uptake compared to unmodified origami and adjust the surface properties of DNA nanostructures [27].

Tetrahedral structures of DNA have also been illustrated to conserve single-strand sequences against nuclease degradation; especially, this kind of structure has been utilized to increase the in vivo circulation half-time of siRNA from 6 to 24 minutes (N3) [28] and deliver Guanosine-phosphate-(Cytosine GpC) to reduce an immune response (N4) [29]. Finally, highly biocompatible tethered-aptamer nano train of DNA (N5) versus folic acid receptor showed high antitumor efficacy and minimize the side effects of doxo in a mouse xenograft tumor model [30]. Recent studies show that a half-icosahedral nanostructure (N6) can effectively delivery doxorubicin to hepatic and breast cancer cells. The study displayed that the importance of structure and the shape of DNA nanostructures for biomedical applications [31].

Conclusion

The applications of DNA nanotechnology were reviewed in this paper. Through Watson-Crick base pair of DNA can self-assemble to become a functional nanostructure, which has been vastly used for targeted drug delivery and imaging of cancer cells. Moreover, by appointing a various of nanomaterials, such as, fluorescent nanoparticles, nanosheets, gold nanomaterials and magnetic nanoparticles, DNA can be more efficiently utilized in cancer therapy and diagnosis, with minimize risk to be degraded by intracellular nuclease. In the near future, it is assured that more and more intelligent and functional nanomaterials based on DNA will be developed for cancer therapy and diagnosis. Despite the ingrained disadvantages of DNA-based nanomaterials, such as poor efficacy of transport, induction of undesired immune responses, and poor stability in the tumor environment, great advances have already been made to cope these challenges so to achieve early tumor diagnosis and accurate treatment in a near future. In the meantime, it is clear that more efforts should also be dedicated for the improvement of the stability and safety of DNA-based nanomaterials.

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