Biomedical Nanotechnology and Nanomedicine

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Introduction to nanotechnology

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Abstract

This paper is about biomedical nanotechnology and nanomedicine. This paper will introduce the targeted drug delivery and DNA nanotechnology. Examples in this paper will help us to understand what biomedical nanotechnology is. And help us to know why nanotechnology is important in medical.

Targeted drug delivery

Introduction

Targeted drug delivery, is a method of delivering medication to a patient in a manner that increases the concentration of the medication. The goal of a targeted drug delivery system is to prolong, localize, target and have a protected drug interaction with the diseased tissue. The conventional drug delivery system is the absorption of the drug across a biological membrane, whereas the targeted release system is when the drug is released in a dosage form. The advantages to the targeted release system is the reduction in the frequency of the dosages taken by the patient, having a more uniform effect of the drug, reduction of drug side effects, and reduced fluctuation in circulating drug levels. The disadvantage of the system is high cost which makes productivity more difficult and the reduced ability to adjust the dosages.

Targeted drug delivery systems have been developed to optimize regenerative techniques. The system is based on a method that delivers a certain amount of a therapeutic agent for a prolonged period of time to a targeted diseased area within the body. This helps maintain the required plasma and tissue drug levels in the body. It can avoid any damage to the healthy tissue via the drug. The drug delivery system is highly integrated and requires various disciplines, such as chemists, biologist and engineers, to join forces to optimize this system.

Chitosan-surface modified poly (lactide-co-glycolide)

Acidic pH is regarded as a characteristic of cancer tumors. Under this acidic condition, the surface charges of Chitosan-modified nano-particles become more positive. Cancer cells are negatively charged. We can load anticancer drugs into this targeted drug delivery system. A strong electrostatic interaction between negatively charged tumor cells and positively charged nano-particles will be obtained.

Chitosan chemical structure:

Chitosan-surface modified poly NPs were optimized as a potential carrier for drug delivery. Chitosan can be put into or onto Poly by three methods:

1. Use of an acidic aqueous solution of Chitosan during the emulsification step used to prepare poly particles
(2) Coating the surface of the poly particles or films using an aqueous solution of Chitosan

(3) Chemical conjugation of Chitosan to the poly particles or films using cross-linkers such as, carbo-di-amide.

a) nano-particles sample
b) nano-particles with 0.02% Chitosan
c) nano-particles with 0.1% Chitosan.

In this example we combine Chitosan poly and drug together. Chitosan-surface modified poly regard as container of the drug. We use electrostatic interaction to “find” cancer cells.

**Temperature-sensitive nanocapsule for drug delivery**

Designing of the technology in targeted drug delivery is critical for the treatment of such conditions as cancer. The application of regular medications in chemotherapy has many side effects, since they affect not only ill cells, but also healthy ones as well. The limited effect on healthy cells is the task solved with the targeted drug delivery. By eliminating the drug effect on healthy cells, it is possible to apply higher concentrations of regular medications or stronger medications with higher quality effect on sick cells. Materials, from the perspective of drug delivery, include polymer nanoparticles, polymer micelles, dendrimers, liposomes, viralbased nanoparticles and carbon nanotubes. Nanotubes and their derivatives are biocompatible materials and can be applied as drug delivery means. The medication can be fixed either inside or outside a nanotube. After the intake into the human body intravenously or
orally, the medication can be ejected by changing the medium pH factor, temperature, under electric-field action, light illumination or particle-activator.

In the example of doxorubicin, it is demonstrated that the nanocapsule stores the drug at normal human body temperature (36.68°C). During the short-time heat action, the gas inside the nanocapsule expands. The gas pushes the fullerene-piston, which ejects the doxorubicin molecule out of the nanocapsule. The heat action is achieved by elevating the temperature of the system simulated by 7 that can be reached with infrared radiation in the target region. The use of such nanocapsules is a new way in drug delivery, which significantly decreases the influence of side-effects and strictly controls the area of curing. Also, the use of heat action as a trigger gives an opportunity to take no other particle-activators for drug release.

Fullerene C60 acts as a trigger in the nanocapsule blocking helium in carbon capsule formed from the nanotube. For helium not to eject C60, there is an chamber with the diameter d3. Fullerene C240 acts as a piston when ejecting the drug.

This region, containing fullerene C60. C60 potential energy that changes with respect to its position in the nanocapsule. The minimum value of potential energy reaches -95.78 kcal/mol. This potential pit is required to keep C60 between the region of helium storage area and intermediary chamber.

1 – nanocapsule
2 – helium atom
3 – fullerene C60
4 – fullerene C240
5 – doxorubicin molecule

d1 – 5.3 nm
d2 – 1.36 nm
d3 – 2.68 nm
d4 – 2.06 nm
This region, containing fullerene C240. C240 potential energy that changes with respect to its position in the nanocapsule are shown in this picture. The minimum value of potential energy reaches -252 kcal/mol.

When the system temperature rises by 7°C, the kinetic energy of atom motion increases, and helium pressure inside the nanocapsule goes up. The gas pressure is sufficient for C60 to overcome the energy barrier and move into the intermediary chamber.

C60 moves along the nanocapsule wall that is more favourable from the energy point. At 12 ps C60, hitting against the nanocapsule walls, loses its kinetic energy.

Under the pressure of helium atoms, the kinetic energy increase (peak N3). The movement continues up to 17.5 ps. The acting capillary forces of the chamber prevent C60 from moving to the region of the nanotube.

The dropping of helium pressure is not that high to overcome these forces, therefore C60 moves from the nanotube to the chamber centre with the kinetic energy increase (peak 4). Then C60 is stable.
Helium molecules press the fullerene C240 and try to push it out of the nanocapsule. Fullerene C240 movement and change in its kinetic energy are shown in this picture. We can see the position of C240 in the nanocapsule and that the drug molecule is located outside. During the same time interval, the oscillations of kinetic energy fade to 0.01 eV. Helium pressure is not sufficient for C240 to overcome the energy barrier and leave the nanocapsule.

DNA nanotechnology

Introduction

DNA nanotechnology is the design and manufacture of artificial nucleic acid structures for technological uses. In this field, nucleic acids are used as non-biological engineering materials for nanotechnology rather than as the carriers of genetic information in living cells. This use is enabled by the strict base pairing rules of nucleic acids, which cause only portions of strands with complementary base sequences to bind together to form strong, rigid double helix structures. This allows for the rational design of base sequences that will selectively assemble to form complex target structures with precisely controlled nanoscale features. DNA is the dominant material used, but structures incorporating other nucleic acids such as RNA and peptide nucleic acid (PNA) have also been constructed, leading to the occasional use of the name nucleic acid nanotechnology to describe the field.

The conceptual foundation for DNA nanotechnology was first laid out by Nadrian Seeman in the early 1980s, and the field began to attract widespread interest in the mid-2000s. Researchers in the field have created both static structures such as two- and three-dimensional crystal lattices, nanotubes, polyhedra, and arbitrary shapes; and functional structures such as molecular machines and DNA computers. A number of assembly methods are used to make these structures, including tile-based structures that assemble from smaller structures, folding structures using the DNA origami method, and dynamically reconfigurable structures using strand displacement techniques. The field is beginning to be used as a tool to solve basic science problems in structural biology and biophysics, including applications in crystallography and spectroscopy for protein structure determination. Potential applications in molecular scale electronics and nanomedicine are also being investigated.

DNA

DNA is a molecule that encodes the genetic instructions used in the development and functioning of all known living organisms and many viruses.
Genetic information is encoded as a sequence of nucleotides (guanine, adenine, thymine, and cytosine). DNA backbone is resistant to cleavage and the double-stranded structure provides the molecule with a built-in duplicate of the encoded information.

Properties of nucleic acids

DNA nanotechnology, specifically, is an example of bottom-up molecular self-assembly, in which molecular components spontaneously organize into stable structures; the particular form of these structures is induced by the physical and chemical properties of the components selected by the designers. In DNA nanotechnology the component materials are strands of nucleic acids such as DNA, which are well-suited to nanoscale construction because a nucleic acid double helix has a diameter of 2 nm and a helical repeat length of 3.5 nm. The key property which makes nucleic acids more useful for constructing structures than other materials is that the binding between two nucleic acid strands depends on simple base pairing rules which are well understood, and form a specific structure upon binding, making the assembly of nucleic acid structures easy to control through nucleic acid design. This property is absent in other materials used in nanotechnology, including proteins, for which protein design is very difficult, and nanoparticles, which lack the capability for specific assembly on their own.

The structure of a nucleic acid molecule consists of a sequence of nucleotides distinguished by which nucleobase they contain. In DNA, the four bases present are adenine (A), cytosine (C), guanine (G), and thymine (T). Nucleic acids have the property that two molecules will only bind to each other to form a double helix if the two sequences are complementary, meaning that they form matching sequences of base pairs, with A only binding to T, and C only to G. Because the formation of correctly matched base pairs is energetically favorable, nucleic acid strands are expected in most cases to bind to each other in the conformation that maximizes the number of correctly paired bases. The sequences of bases in a system of strands thus determine the pattern of binding and the overall structure in an easily controllable way. In DNA nanotechnology, the base sequences of strands are rationally designed by researchers so that the base pairing interactions cause the strands to assemble in the desired conformation.
Small nucleic acid complexes can be equipped with sticky ends and combined into larger two-dimensional periodic lattices containing a specific tessellated pattern of the individual molecular tiles. The earliest example of this used double-crossover (DX) complexes as the basic tiles, each containing four sticky ends designed with sequences that caused the DX units to combine into periodic two-dimensional flat sheets that are essentially rigid two-dimensional crystals of DNA. Two-dimensional arrays have been made from other motifs as well, including the Holliday junction rhombus lattice, and various DX-based arrays making use of a double-cohesion scheme. The top two images at right show examples of tile-based periodic lattices.

Two-dimensional arrays can be made to exhibit aperiodic structures whose assembly implements a specific algorithm, exhibiting one form of DNA computing. The DX tiles can have their sticky end sequences chosen so that they act as Wang tiles, allowing them to perform computation. A DX array whose assembly encodes an XOR operation has been demonstrated; this allows the DNA array to implement a cellular automaton that generates a fractal known as the Sierpinski gasket. The third image at right shows this type of array. Another system has the function of a binary counter, displaying a representation of increasing binary numbers as it grows. These results show that computation can be incorporated into the assembly of DNA arrays.

DX arrays have been made to form hollow nanotubes 4–20 nm in diameter, essentially two-dimensional lattices which curve back upon themselves. These DNA nanotubes are somewhat similar in size and shape to carbon nanotubes, and while they lack the electrical conductance of carbon nanotubes, DNA nanotubes are more easily modified and connected to other structures. One of many schemes for constructing DNA nanotubes uses a lattice of curved DX tiles that curls around itself and closes into a tube. In an alternative method that allows the circumference to be specified in a simple, modular fashion using single-stranded tiles, the rigidity of the tube is an emergent property.

This is a DNA tetrahedron. Each edge of it is a 20 base pair DNA double helix. Each vertex is a three-arm junction.
This picture is a model of a DNA tile used to make two-dimensional periodic lattice.

Conclusions

Targeted drug delivery can be used to treat many diseases, such as the cardiovascular diseases and diabetes. The most important application of targeted drug delivery is to treat cancerous tumors. The advantages to the targeted release system is the reduction in the frequency of the dosages taken by the patient, having a more uniform effect of the drug, reduction of drug side effects, and reduced fluctuation in circulating drug levels. As the nanotechnology improve, the targeted drug delivery will widely use and cure more disease.

About DNA nanotechnology, in this field, DNA is used as non-biological engineering materials for nanotechnology rather than as the carriers of genetic information in living cells today. In the future DNA nanotechnology will be used in genetically modified and Cure genetic disease.

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