Novel Nanoparticles for Cancer Detection and Prevention

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ABSTRACT

The use of novel materials for drug delivery and therapeutic applications present the potential for eradicating many harmful diseases such as cancer and heart disease. Nanoparticles including quantum dots (QDs) and gold nanoparticles provide a more viable and effective alternative to conventional techniques used for diagnostic and therapeutic applications. An improvement in the accuracy and time of detection of the onset of malignant tumors is necessary to prolong lives of cancer patients.

Quantum dots and gold nanoparticles are excellent for developing bio-chemical sensors against the onset of tumor-associated antigens (proteins). This paper presents a review of the concepts, the design, manufacture and use of quantum dots and gold nanoparticles for detection and prevention of the onset of malignant tumor formation. The intended targets for the elegant nanoparticles and their broader impacts in mitigating malignant tumor formation are discussed.

Keywords: nanoparticles, quantum dots, fluorescent, drug delivery, encapsulated

1 BACKGROUND

Advances in medical technology necessarily depend on our understanding of living systems. There is a growing interest in the myriad of research efforts into the detection and therapeutic treatment of cancer. Extensive studies have shown that the change of a normal cell into a metastatic cancer cell arises due to the accumulation of mutations in tumor suppressors. Various approaches are in vogue that are concerned with mediating in the mechanism of cancer tumor formation and possibly preventing the propagation of the disease [Owusu and Owusu, 2000].

Of particular significance is the emerging field of nanotechnology-based biomedical techniques. These approaches include the development of novel extraneous materials and nanoparticles that are specially designed to probe the embryonic signatures of cancer. In addition, such nanoparticles are engineered to improve the specificity and sensitivity limits of optical imaging capabilities. Nanoparticle-based techniques are a promising novel tool that presents the ability for earlier, faster and more selective diagnosis of cancer at much lower costs and reduced side-effects.

Sokolov et al. [2003] demonstrated the use of gold colloidal formulations that targeted Epidermal Growth Factor Receptor (EGFR) antibodies as scattering contrast agents for optical imaging of cervical cancer cells and tissue specimens. In addition, similar advances including optical imaging applications of nanoparticles have been described by multiple groups including Bruchez et al. [1998], and Akerman et al. [2002].

2 NANOPARTICLES FOR DRUG DELIVERY AND TUMOR DIAGNOSTICS

A variety of nanomaterials are finding viable applications including drug delivery as well as targeting and imaging of the onset of malignant tumor formation in tissues. It is estimated that the global market for drug delivery products is $33 billion per year and growing at a rate of 15% per year [Hill, 2005].

The targeting capability of nanoparticles is influenced by particle size, surface charge, surface modification, and hydrophobicity whilst their general performance in vivo is influenced by morphological characteristics, surface chemistry, and molecular weight.

Recent studies have suggested that nanoparticle drug delivery might improve the therapeutic response to anticancer drugs and allow the simultaneous monitoring of drug uptake by tumors [Kukowska-Latallo et al., 2005]. Drug delivery of anti-estrogens enhances their ability to arrest the growth of tumors which express estrogen receptors and are of particular interest for estrogen-dependent breast cancer treatment. In addition, it represents a new potent therapeutic approach for multiple myeloma [Maillard et al., 2005]. The predominant challenge associated with the synthesis and use of nanoparticles after their preparation is their chemical stability. This concern is addressed, by and large, by freeze-drying using different classes of lyoprotectants.

A novel preparation method for core / shell nanoparticles with a drug-loaded lipid core was designed and characterized by Oh et al. [2005]. For the application of the core/shell nanoparticles as a drug carrier, paclitaxel, a potent anticancer drug, was loaded into the core/shell nanoparticles making it possible to observe the drug release pattern on the nanoparticle [Oh et al., 2005].

3 DESIGN, SYNTHESIS, AND APPLICATION OF ENCAPSULATED QUANTUM DOTS

Research in the design and applications of semiconductor nanocrystals, known as Quantum Dots (QDs) is gaining prominence. Quantum dots are the nanoparticles that are recently emerging as an alternative to organic fluorescence probes in cell biology and biomedicine. QDs are monodispersed semiconductor nanocrystals (Size range 2-10 nm) covered with a stabilizing monolayer. QDs have several predictive advantages such as ability to absorb light within a broad band of wavelength but emit at much narrower bands. QDs have high stability, and possess superior imaging capabilities. These unique properties allow simultaneous excitation of different sizes of quantum dots with a single excitation light source, their simultaneous resolution and visualization as different colors.

When the electrons in a semiconductor are excited, they prefer to dwell at a certain fixed distance from the positive charges they leave behind, called the exciton radius. For the semiconductors used to make fluorescent QDs, this radius is around 5–10 nanometers. If the entire crystal's size is less than the exciton radius, however, an effect called quantum confinement comes into play, and shifts the color of the emitted light towards shorter wavelengths. For crystals of this size, more energy than normal is required to force electrons out of the ground state. So when the electrons return to the ground state, the photons they release have more energy and therefore, a shorter wavelength than normal. There is a simple linear relationship between crystal size and color: the smaller the size, the shorter the wavelength.

In the area of biomedical applications, water-soluble and biodegradable QDs that have been encapsulated with glycopeptides in the form of receptors and ligands have been shown to bind to living cells [Loo et al, 2004]. Recently, highly lumniscent encapsulated cadmium tellurium (CdTe) have been synthesized in a one-pot aqueous synthetic method [Svarovsky and Brachi, 2005]. This novel method involved the use of two symbiotic capping agents; one that promotes the growth and quantum efficiency of the nanocrystals while the other incorporates important biofunctional tumor associated carbohydrate antigens (Figures 1 and 2).

In addition to the attributes above, when QDs are densely populated with tumor-specific saccharides, they bind strongly and specifically with lectins specifically expressed in the malignant tumor sites. Encapsulated QDs can be used to identify diseases in a process similar to currently widely used Magnetic Resonance Imaging (MRI).

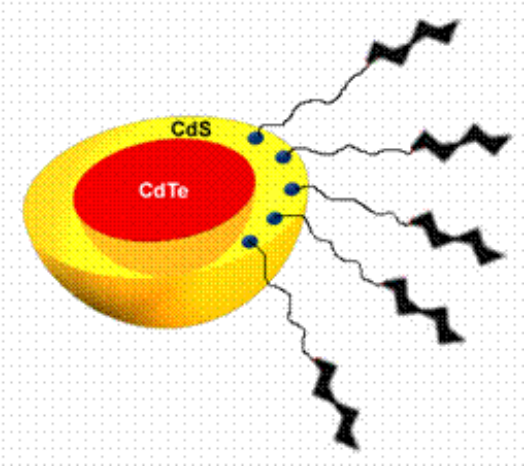

Figure 1: Quantum dots showing CdTe core and CdS shell formation. The tethers are the ligand attachments [Svarovsky and Barchi, 2005].

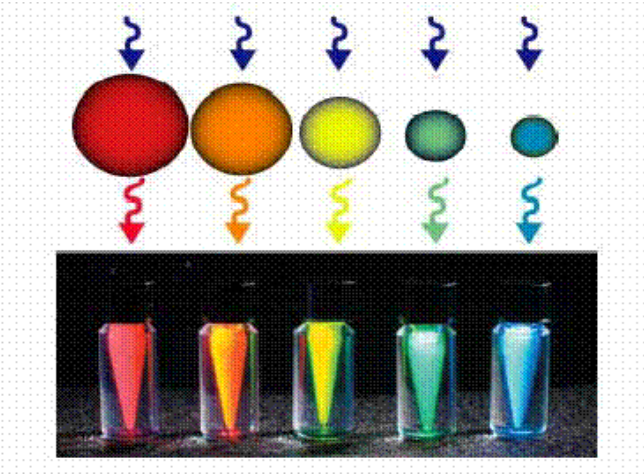

Figure 2: Schematic representation of the effect of size on the color of QD particles. Five different QD solutions can be excited with a single wavelength [Svarovsky and Barchi, 2005].

QDs can significantly improve clinical diagnostic tests for the early detection of malignant tumors. QDs acting as multivalent fluorescent tags (Figure 3) can be used to seek out specific lectins and antibodies in a multiplex fashion to detect various disease states or harmful pathogens simultaneously in high throughput medical diagnostics.

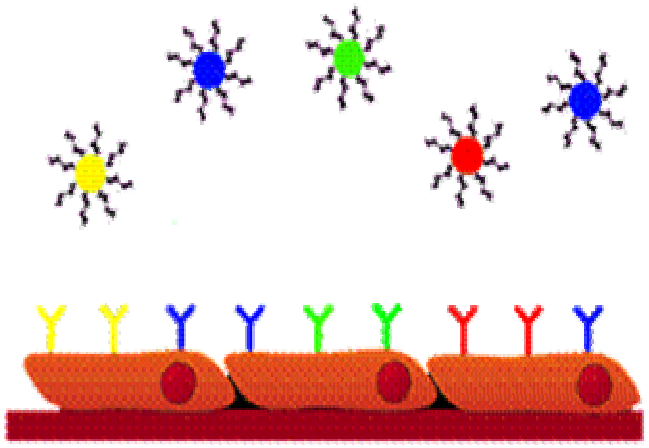

Figure 3: The multivalent fluorescent tagging property of QDs.

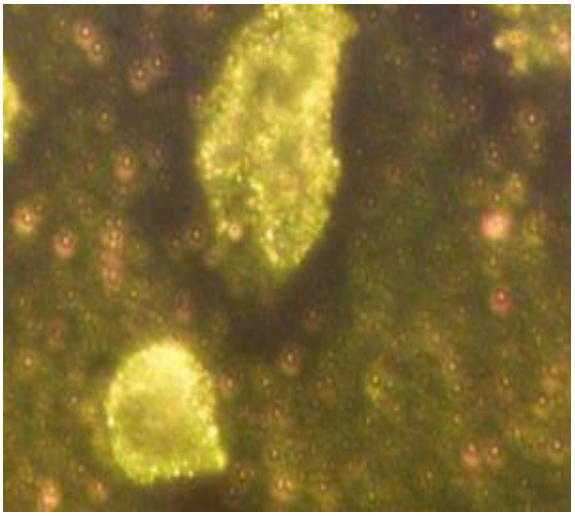

Figure 4: SEM image showing the high affinity of gold nanoparticles for cancer cells. The gold nanoparticles stick to cancer cells and make them shine [El Sayed, (Georgia Tech), 2005].

4 DESIGN, SYNTHESIS, AND APPLICATION OF GOLD NANOPARTICLES

Due to their biocompatibility and excellent optical properties, gold nanoparticles are finding increasing application in a variety of areas including DNA detection and cancer diagnostics. They are also useful for identification of protein-protein interactions [Salata, 2004]. They are non-toxic in vivo, maintain their biofunctionality in vitro, possess high degree of multivalency and have high biological stability against enzyme degradation. Gold nanoparticles functionalized with oligonucleotides have been used as probes in DNA detection [Sau et al, 2001], [Daniel and Astruc, 2004].

According to researchers from the University of California and Georgia Institute of Technology, gold nanoparticles could be bound to malignant cancer-prone cells, thereby causing easy detection. The gold nanoparticles can be conjugated to an antibody for epidermal growth factor receptor (EGFR) proteins. These EGFR cells which are found on the surface of most cancer cells respond to the presence of gold due to the ability of the gold nanoparticles to absorb light. Figure 4 shows the optical effect of gold nanoparticles on cancer cells due their high affinity for cancer cells.

The stability of gold nanoparticles can be achieved through the use of stabilizers such as gelatin [Bhaskaran, 2005]. In addition to these developments, colloidal gold nanoparticle platforms have been designed and used as a tumor targeting ligand and a cancer therapy [Paciotti et al., 2005].

Numerous methods of manufacturing gold nanoparticles involve wet chemistry techniques. Prominent among such methods is the chemical reduction of gold using sodium borohydride as a reducing agent. Small spherical particles of average diameters between 5 and 20 nm have been prepared by UV radiation of gold ions. Larger particles (20 – 110 nm) have been formed by irradiation coupled by reduction with absorbic acid [Sau et al., 2001].

5 TARGETS

Diseases that can result from defective genes span a wide range. Examples include: cancerous, infectious, cardiovascular, and monogenic (i.e. hemophilia) diseases, and rheumatoid arthritis. Gene therapy is a recently introduced method for treatment or prevention of genetic disorders based on delivery of repaired, or the replacement of incorrect, genes. It is aimed at treating or eliminating the causes of disease, whereas most current drugs treat the symptoms.

Delivery of repaired genes, or the replacement of genes, is a field where nanoscale objects could be introduced successfully. Nanoparticle vector genetic immunization would also have a number of potential advantages over conventional vaccines, These include: (i) the high stability of plasmid DNA, (ii) low manufacturing costs, (iii) reduction in the risk of infection associated with attenuated viral vaccines, (iv) the capacity to target multiple antigens to one plasmid, and (v) the ability to elicit both humoral and cellular responses.

6 CONCLUSION

In addition to the conventional benefits one receives from an innovative product or technology such as costs to consumer and producer, the use nanoparticles has and is continuing to revolutionize the field of medicine on a variety of fronts including: non-invasive and improved drug delivery, improvement in patient adherence to drug regimens, and the use of biomolecules that we were previously unable to administer.

The state of health for individuals will increase and life spans will improve. Health improvement and lifespan extension do not depend on nanoparticles, but nanoparticles will certainly make them accessible to more people. Any treatment that can be automated can be applied to a vast number of people economically. Efficient research will accelerate the development of cures for complex problems such as cancer, asthma, heart disease, and Parkinson's disease. New therapeutic techniques will allow the treatment of many types of diseases, which previously were too expensive and complicated to research. Using such non-invasive routes eliminates the need for administration of drugs by injection. The development of nanoparticles for improved release rates and bioavailability will significantly reduce the amount of dosage previously required.

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