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Gold nanoparticles: Optical properties, Applications in Cancer Diagnosis and Therapy !!

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Abstract :

Almost 4 decades have passed since the "war on cancer" was declared. This is nowgenerally believed that personalized medicine was the future of cancer treatment.It has unprecedented potential for early detection, accurate diagnosis and personalization For the treatment of cancer, nanoparticles have been intensively studied in the last decade. In this overview, we will summarize the current state of gold nanoparticles in biomedicine applications targeting cancer. Gold nanospheres, nanorods, nanoshells, nanoparticles and surface Nanoparticles with enhanced Raman scattering will be discussed in detail regarding their applications in in vitro assays, ex vivo and in vivo imaging, cancer therapy and drug delivery. Multifunctionality is a key property of nanoparticle-based materials. Targeting ligands, imaging labels, therapeutics drugs and other functions can all be integrated to enable targeted molecular imaging and molecular cancer therapy. Great advances and many proofs of principle have been made studies have been successfully conducted. The future looks brighter than ever, but obstacles abound remains to be conquered. A multifunctional gold nanoparticle-based platform with enhanced receptor targeting, multimodality imaging, and multiple therapeutic entities holds promise for a "magic golden bullet" against cancer.

Keywords :

cancer ,golden bullet, nanospheres, nanorod , gold nanoparticles, multimodality imaging, therapy

Introduction

Cancer is the third leading cause of death (after heart disease and stroke) in the developed world countries and the second leading cause of death (after heart disease) in the United States states (see http://www.cdc.gov). Studies have shown that there were 10 million new ones cases, 6 million deaths and 22 million people living with cancer worldwide year 2000 (Parkin 2001). These figures represent an approximately 22% increase in incidaily and mortality since 1990 (Parkin et al. 1999; Pisani et al. 1999). The

number of new cases of all cancers worldwide is projected to be 12.3 a15.4 million in 2010 and 2020 (Parkin 2001). In 2008 in total 1,437,180 new cancer cases and 565,650 cancer deaths are estimat

ed cancer treatment (Cai and Chen 2007). Nanoparticles they are typically smaller than a few hundred nanometers, comparable to large ones biological molecules such as enzymes, receptors and antibodies. With size about one hundred to ten thousand times smaller than human cells, these nanoparticles can offer unprecedented interactions with biomolecules and of inside cells, which may revolutionize cancer diagnosis and treatment. Among the most studied nanoparticles are quantum dots (Cai et al 2006, 2007b), carbon nanotubes (Liuet al 2007b), paramagnetic nanoparticles (Thorek et al 2006),liposomes , gold nanoparticles and many others (Ferrari 2005; Grodzinski et al2006)(figure 01)

Many nanotechnologies have emerged over the past decadeogy centers established around the world (Kawasaki and Player 2005; Horton and Khan 2006). Only in the United States more than six billion dollars have been invested in nanotechnology technological research and more than sixty centers, networks,and facilities funded by various agencies are in operation or open early (Thayer 2007). After establishing between disciplinary workforce in nanotechnology is expected nanotechnology matures into a clinically useful field near future. One of the main applications of nanotechnology is in biomedicine. Nanoparticles can be constructed as a nanoplate forms for efficient and targeted drug administration and imaging brands by overcoming many biological, biophysical and biomedical barriers. For in vitro and ex vivo applications, advantages of state-of-the-art nanodevices (e.g. nanochips and nanosensors) over traditional testing methods are obvious (Grodzinski et al. 2006; Sahoo et al. 2007). However, a few there are barriers to in vivo applications in preclinical and potential clinical applications of nanotechnology, which include biocompatibility, in vivo kinetics, tumor targeting efficacy irritation, acute and chronic toxicity, ability to escape from the network endothelial system (RES) and cost-effectiveness (Cai a Chen 2007, 2008). In this review, we summarize current status of gold nanoparticles in biomedicine applications.

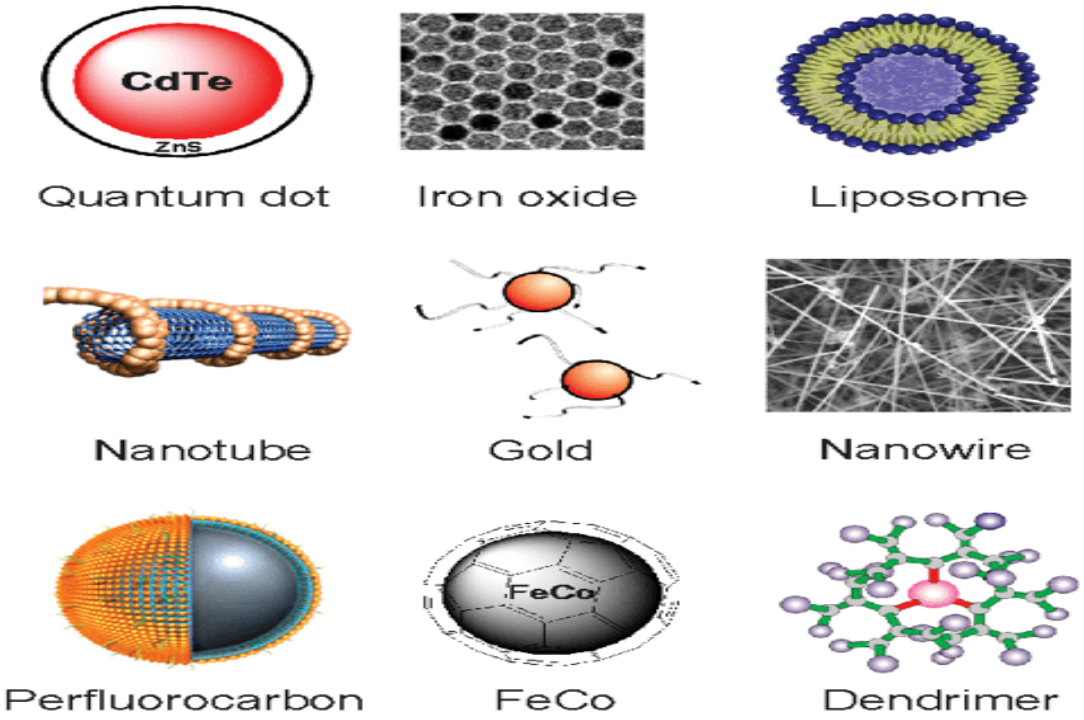

Figure 1:different nanoparticles for detection & treating cancer.

Synthesis of goldnanoparticles:

There are many subtypes of gold nanoparticles based on size, shape and physical properties (Figure 2). First the studied gold nanoparticles are gold nanospheres (although not precisely spherical in the strict sense of the word). Subsequently, nanorods, nanoshells and nanoparticles have been reported. Next a type of gold-based nanoparticles with an excellent surface enhanced Raman scattering properties (referred to as “SERS nanoparticles”), will also be discussed in this review. IN the term "gold nanoparticles" will be referred to below. a collection of all these subtypes and a gold subtype the nanoparticles used in each study will be specified at any time possible. With continued developments in synthesis techniques over the past two decades, most of these gold nanoparticles can now be produced with well-controlled size distribution, sometimes with stunning accuracy (e.g. nanoparticles).

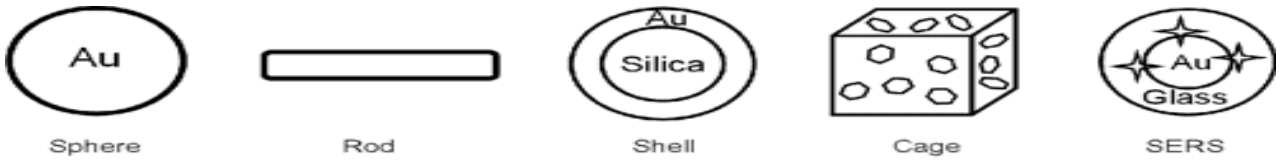

Figure: synthesis of gold nanoparticles

Gold nanoparticles:

Improved photophysical properties gold nanoparticles When matter is exposed to light, the line processes may occur:

• Light can be absorbed

• Light can be scattered just as freely quence as incoming light (Mie or Rayleigh dispersion)

• Absorbed light can be re-emitted (ie fluorescence)

• The local electromagnetic field of the incoming signal

light can be amplified, thereby enhancing any spectroscopic signals from molecules in material surface i.e. surface enhanced specification troscopy such as surface-enhanced Raman distraction.

In the case of gold nanoparticles, all these proes are greatly enhanced by uniqueness interaction of light with free electrons metal particles. When the nanoparticles are gold exposed to light radiation, electric field the light causes a collective oscillation of the line electrons in the thion band on the surface of the particle,with respect to the ionic core nanoparticles . Coherent oscillation metal-free electrons in resonance with electrons magnetic field is called surface plasmon resonance (SPR). Theoretical and experimental a discussion of SPR can be found in earlier a more recent literature. For gold nanospheres,this resonance occurs in the visible region of the spectrum at about 520 nm, which is the origin the bright red color of nanoparticles in solution her. In gold nanorods, free electrons oscillate along the long and short axis of the nanorods [resulting in a stronger resonance band nearby infrared (NIR) regions and a weaker v band visible area (similar to nanospheres), or tively . SPR excitation results in the improvement of photophysical properties bonds of gold nanoparticles.

Light scattering imaging

Rayleigh (Mie) scattering by gold nanoparticles Ticles is greatly enhanced due to excitation SPR . Free Scattering SPR frequency and intensity are sensitive to size, shape, composition and environment of nanparticles and can be quantified using Mie theory for spherical gold nanoparticles. Typically, these are nanoparticles with a diameter of 30–100 nm scatters intensely and can be easily detected and commercial microscope under dark field illumination national conditions . In fact, 40 nm gold nanoparticles can be easily detected by eye, up to a particle concentration 10-14 M . Likewise, scattering from a 60 nm gold nanoparticle Ticle is 105 stronger than emission a fluorescein molecule .The light scattering of gold nanorods depends on ent heavily on aspect ratio nanorods. With increasing aspect ratio longitudinal band intensity ratio to that of the transverse band increases a SPR maximum longitudinal mode red displacements, while for transverse mode blue moves only slightly. Wavelength shift the longitudinal band depends linearly on the nano rod aspect ratio [94]. Recently, El-Sayed et alleagues calculated the size and shape dependence contribution of SPR variance to total extinction (sum of absorption and scattering) using the discrete dipole approximation method [95,96]. Scatter to extinction the ratio increases with increasing size nanospheres and nanorods that enable according to the choice of gold nanoparticles for either optimized imaging or photothermal therapy.Cross-sections of gold with high dispersion nanoparticles along with their excellent permanence (compared to organic dyes), to be powerful for imaging-based medicine applications. Using light scattering property of gold nanoparticles for cellular imaginging, especially cancer imaging, has advanced inrecent years.

Study by Sokolov et al. showed that gold nanoparticles can be molecularly targeted to cancer cells and tissues by conjugation with antiepidermal growth factor antireceptor (anti-EGFR) antibodies . The cells or tissue labeled with an antibody-conjugated gold nanoparticles can be clearly visualized by SPR scattering of nanoparticles under monochromatic lighting using scanning ning laser-confocal reflection microscope or even light from a simple laser pen. The strong scattering from gold nanoparticles thus providing effective optical marking cancer biomarkers.

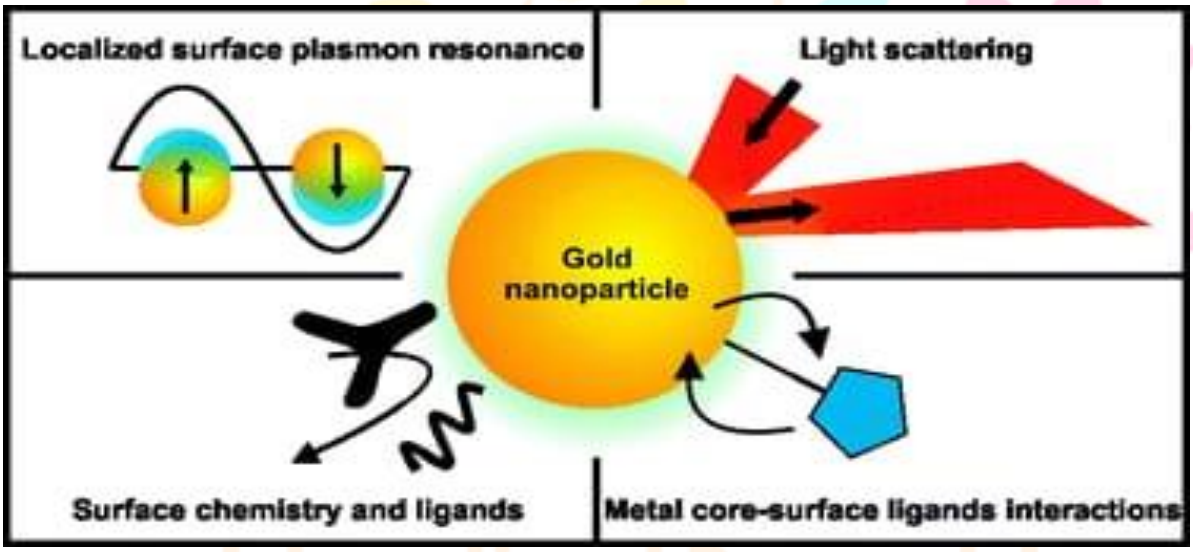

Fig 3:- scattering of goldnanoparticles

- **SERS nanoparticles**

  SERS is an optical technique that offers many advantages versus traditional technologies such as fluorescence and chemiluminescence, including better sensitivity, high levelmultiplexing, robustness and superior performance in blood and other biological matrices (Sha et al 2007; Hering et al 2008). In a pioneering report, gold nanospheres (~13 nm in diameter) modified with Cy3-labeled, alkylthiol-capped oligonucleotide chains were used as probes to monitor
  to the presence of specific target DNA strands (Cao et al 2002).

The Cy3 group was chosen as the Raman label because of its large Raman cross section. Subsequently, several other reports have also used SERS nanoparticles. In one study, gold nanospheres (60 nm in diameter) were encoded by a Raman reporter and stabilized coated with a layer of thiolated polyethylene glycol (PEG) (Qian et al. 2008). Another type of nanoparticle is SERS consists of a gold core, a Raman active molecular layer, and silica coating (Keren et al 2008). Silicon dioxide coating can provide physical resistance, inertness to various environments mental states and simple surface treatment using silica chemistry. Thiol groups that were subsequently introduced deposited on a silica shell can be conjugated with maleimide activated PEG chains for improved biocompatibility.

- **Application of nanoparticles**

Nanotechnology is a very hot topic last decade. A simple search for "Nano" in PubMed returned more than 6000 publications. Two main areas applications of nanoparticles are materials science and biomedicine cinema. Great strides have been made in materials science arena. The fact that electronics are getting faster, better, and smaller each month is a clear and strong proof such an achievement. However, the application of nanoparticles in the field of biomedicine did not meet expectations. Very few nanoparticle-based agents are in clinical testing or commercialized for the diagnosis or treatment of cancer and most of them are based on liposomes that have been developed several decades ago. We still have a long way to go nanotechnology can truly revolutionize patient care many hoped so. Next, we summarize progress to date in the use of gold nanoparticles for biomedical applications.

- **In vitro tests by goldnanoparticles:**

Gold nanoparticles coated with oligonucleotides were reported for a polynucleotide or protein (such as p53, tumor suppressor gene) detection using different detections/traits terization methods such as atomic force microscopy (AFM) (Han et al. 2000; Jin et al. 2007), gel electrophoresis (Qin and Yung 2007), scanometric test (Son and Lee 2007), chronoculometry (Zhang et al 2007), amplified voltammetry detection (Wang et al 2008a), SPR imaging (Li et al 2006), and Raman spectroscopy (Cao et al 2002). In some reports picomolar and femtomolar concentrations of DNA targets have been discovered. A bifunctional adsorbate based on DNA molecules were evaluated as molecular rulers, based on SERS signals that vary independently in intensity as function of the distance from the surface of the gold nanoparticle (Lal et al 2006). Gold nanoparticles have also been used for many other applications such as immunoassay (Hirsch et al 2003a, 2005; Liu et al. 2008), protein assay (Tang et al. 2007), secondary ion-of-flight mass spectrometry (Kim et al 2006), capillary electrophoresis (Tseng et al 2005) and detection cancer cells (Kah et al. 2007; Medley et al. 2008). In one report, dynamic light scattering (DLS) enabled quant estimation of the concentration of intravenously administered gold nanoshells in mouse blood (Xie et al 2007). This technique can also be used to estimate circulations lifetime of other solid nanoparticles. Gold nanoshells functionalized with a pH-sensitive SERS reporter molecule, 4-mercaptopyridine, have been shown to be pH responsive ambient media in the range of 3 to 7 (Jensen et al 2007). Another study evaluated the use of gold nanoshells as optical biosensors for the real-time detection of streptavidin biotin interactions in diluted human blood (Wang et al 2008b). However, both the sensitivity (~3 ug/ml) and the dynamics range (3–50 µg/ml) were very poor.In many cases, literature reports have mixed results. It will be ideal if different tests can be compared side by side using the same model system that can help greatly in deciding which tests are the best candidates for potential clinical testing . National Cancer Institute (NCI) Alliance for Nanotechnology in Cancer each of its funded centers to test its newly developed nano sensors using the same standard samples, which is expected easily identify which new sensors really stand out a large number of new molecular sensors. Extension of similar standard for a much wider range of research laboratories across the country would be very beneficial for cancer patients. Choosing the right candidate at an early stage will not only save money valuable time, but can also dramatically reduce costs development of new tests.

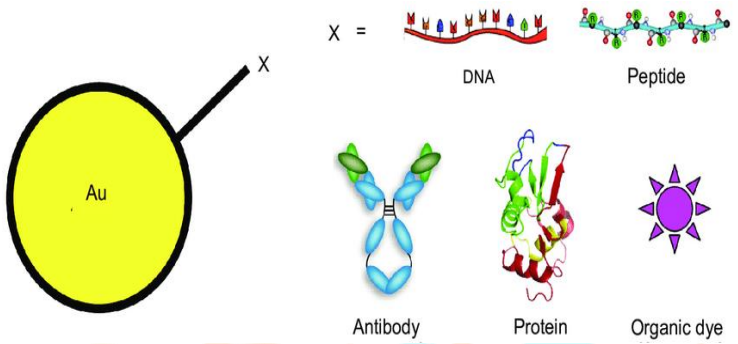

Figure 4: Gold nanoparticles with modified by various molecules in vitro assays.

- **In vivo imaging**

Many paramagnetic nanoparticles have been usedmagnetic resonance (MR) imaging, both preclinical and clinically .Recently, Au3 Cu1nanoshells have been reported to be able to enhance in vivo blood vessel contrast that suggested their potential use in MR angiography as a blood supply agent (Su et al 2007). Due to the low sensitivity of MR imaging, the dose-dependent toxic effect of the nanoshells was observed: 17% of mice died at 20 mg/kg. A self-quenched and protease-sensitive gold nanosphere extinguished probes have been shown to allow visual monitoring activities of both proteases and protease inhibitors v in vitro and in vivo (Lee et al 2008). This technique can also be applied to other proteases using the appropriate peptide substrate as a spacer as previously demonstrated by others studies that used self-extinguishing properties organic fluorescent dyes .Raman spectroscopy is the most promising imaging technique for contrast agents based on gold nanoparticles.Raman spectra and Raman images of methylene blue molecules adsorbed as a single layer on gold nanospheres have been found useful for studying plasmon properties (Laurent et al. 2005). Later, antibody conjugated gold nanorods have been reported to provide a Raman spectrum that is large amplified, sharpened and polarized (Huang et al 2007a). in In these two reports, Raman imaging was tested in cells, but not in living things. Recently, two groups have separated from each other dentally described in vivo targeted cancer imaging using Raman spectroscopy and nanoparticle SERS. First reports, it has been shown that small molecule Raman reporters(such as fluorescent dyes) were stabilized by thiolated PEG and provided large optical enhancements (Qian et al 2008). When conjugated with tumor-targeting ligands, conjugation occurred SERS nanoparticles were able to target tumor markers such as the human epidermal growth factor receptor (EGFR). cancer cells and in xenograft tumor models. Interestingly, although Raman spectra of SERS nanoparticles were reported, the Raman image was not obtained for tumor-bearing mice. In the second study, SERS nanoparticles composed of gold core, Raman active molecular layer and silicon dioxide coating was used for in vivo Raman imaging(Keren et al. 2008). Minimum detection sensitivity 8 picomolar SERS nanoparticles were observed for livelihood mouse. As proof of principle in vivo multiplex imaging of four different SERS nanoparticles.Raman imaging has significant potential as a strategy for biomedical imaging of living subjects. However, one must keep in mind that optical imaging in mice cannot be directly scaled to in vivo imaging in human applications due to the limited penetration of the optical signal into the tissue. in clinical setting, optical imaging (including Raman spectroscopy) is only relevant for tissues close to the surface skin (eg breast imaging), tissues accessible endoscopy (such as esophagus and colon) and intraoperative visualization (typically image-guided surgery). NIR Optical imaging devices for breast detection and diagnosis cancer has been tested in patients and the first results are encouraging (Taroni et al 2004; Intes 2005). More SERS nanoparticles with different absorption wavelengths in the NIR region that can enable multiplexed imaging many tumor markers simultaneously if targeting is effective can be achieved may have significant clinical

potential applications. Imaging devices used in these two studies are non-commercial prototype systems. A lot of future improving both the imaging system and the production/earlier, SERS nanoparticmodification will be required Raman imaging can become a clinical reality.

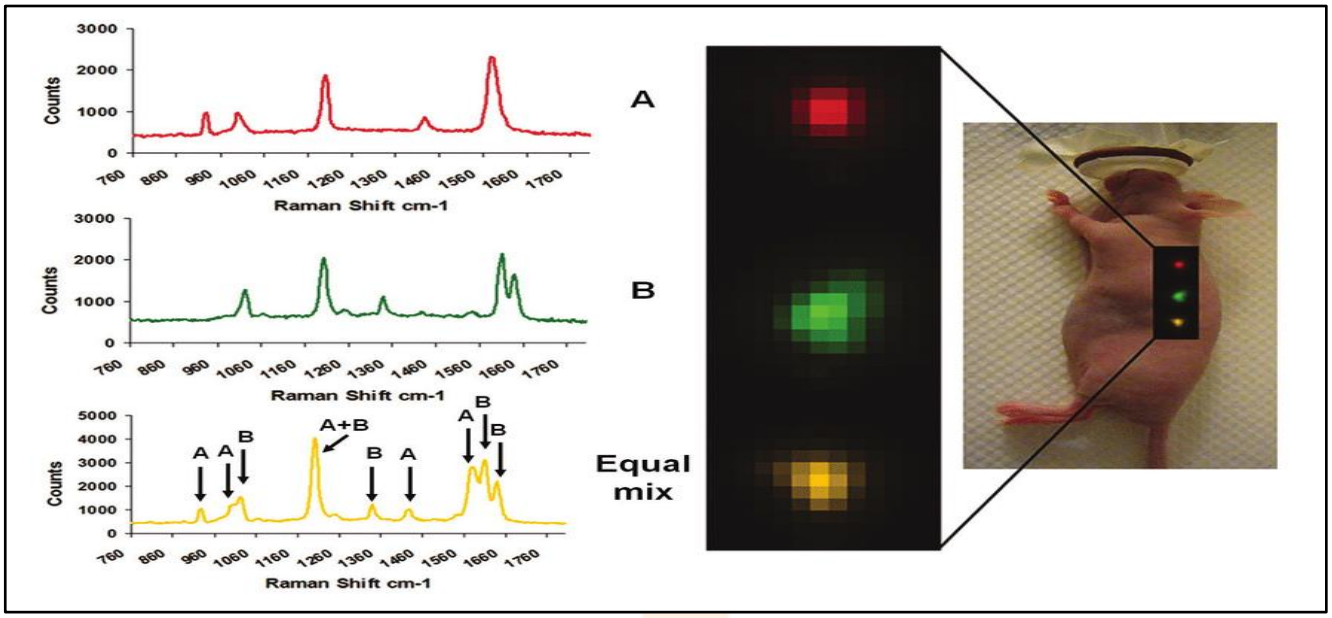

Figure:The in vivo Raman experiment using SERS nanoparticles. Copyright © 2008, PNAS. Adapted with permission from Keren S, Zavaleta C, Cheng Z, et al. 2008. Noninvasive molecular images of small living subjects using Raman spectroscopy.

- **Cancer treatment**

Conventional strategies for cancer treatment include surgery, chemotherapy and radiation therapy. take advantage of their unique properties, most gold studies. Nanoparticle-based cancer treatment uses photothermal therapy to destroy cancer cells or tumor tissue, which may be potentially useful in the clinical setting. When irradiated with laser pulses of perticular specific wavelength, to selected gold nanospheres, nanorods, nanoshells and nanocages can kill bacteria and cancer causing cell. It was estimated that 70–80 °C was achieved by light absorption by gold nanoparticles (Huang et al 2006b) and up to 150 antibodies can be conjugated to the nanoshell via bifunctional PEG linker (Lowery et al 2006). One interesting observation is that most of these studies have focused on either EGFR or humans epidermal growth factor receptor 2 (HER2), apparently as a result to the easy availability of monoclonal antibodies (already approved by the Food and Drug Administration [FDA] for cancer therapy) that recognize these two proteins.Because the absorbance wavelength (in the visible region) of small gold nanospheres is not optimal for in vivo applications. It was found that the formation of nanoclusters led to increased local absorption and redshift compared to cells that did not have nano clusters. Significant enhancement in laser-induced cancer cell killing was observed using a NIR laser. Gold nanoshells are large enough (about 100–300 nm in diameter). In one pioneering study, human breast cancer cells incubated with gold nanoshells were found to be subject to photothermally induced morbidity after exposure to NIR light (Hirsch et al 2003b).In vivo testing has shown that exposure to low dose NIR light in solid tumors treated with gold nanoshells resulted in significant averag temperature increase, capable of causing irreversible tissue damage, while controls (untreated with nanoshells) showed a

much lower average temperature when exposed to NIR light and appeared undamaged (Hirsch et al 2003b). In a recent report it was suggested that 5000 gold a nanoshell per prostate cancer cell was needed to achieve killing cells (Stern et al 2007). PEG-coated nanoshells with a peak absorption in the NIR region were injected intravenously into tumor-bearing nude mice (O'Neal et al 2004; Stern et al 2008). In one study, all tumors were treated with a NIR laser were removed and the mice appeared tumor-free for several months while tumors in control animals (NIR laser treatment without nanoshell injection) continued to grow. In another study, 93% of tumor necrosis and regression was observed in high group treated with a nanoshell dose (8.5 µl/g) (Stern et al 2008). Surprisingly slightly lower dose of nanoshell (7.0 µL/g) only resulted in tumor growth arrest at 21 days, but no tumor ablation. The reason why such a

subtle difference in dose of nanoshell could produce a dramatically different therapy efficacy deserves careful examination. This is worth noting all of these in vivo cancer therapy studies involve only passive tumor targeting but not specific molecular targeting. Passive tumor targeting is due to non-specific accumulation nanoshells in the tumor, called "increased permeability".and retention (EPR) effect" because the tumor vasculature is usually more leaky than normal blood vessels and does not exist lymphatic drainage in the tumor (Maeda et al 2000). Monocyte recruitment to hypoxic areas within of tumors was used for photo-induced cell killing with gold nanoshells (Choi et al 2007). In addition to photothermal gold nanoparticles have also been investigated as therapies further therapeutic studies. Phthalocyanine (photosensitizer) stabilized gold nanospheres (2–4 nm in diameter). reported for photodynamic diagnosis of cultured cancer cells. It has been shown that gold nanoparticles enhance antiproliferation and apoptosis of human hepatitis toma cells induced by paclitaxel, a chemotherapy drug (Wei et al 2007). A recent study showed that an increase in radiosensitivity can be achieved by increasing absorption of ionizing radiation by gold nanoparticles, which in turn caused breaks in single- and double-stranded DNA (Zheng et al 2008). Although it was suggested DNA targeting of cancer cells using gold nanoparticles may offer a new approach that is generally applicable treatment with external radiotherapy, reaching DNA in vivo targeting is extremely difficult.

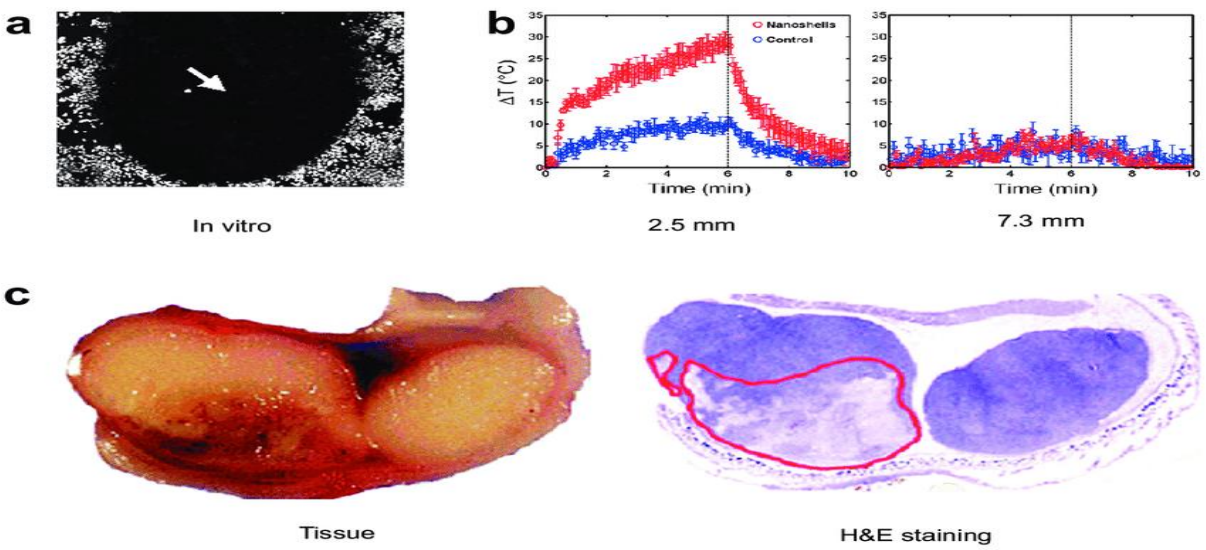

Figure: Gold nanoparticles can destroy cancer cells in vitro and in vivo. A. Cells incubated with gold nanoshells can be killed by NIR light (dark region). b. Time parcels maximum temperature change of NIR-irradiated tumors with and without nanocases at depths of 2.5 mm and 7.3 mm below the tissue surface. C. Gross pathology after in in vivo treatment with nanoshells and NIR laser revealed hemorrhage and loss of tissue birefringence below the apical tissue surface. Hematoxylin/eosin (H&E) staining.the same plane confirms tissue damage in the area that contains the nanoshells. Magnetic resonance-guided nanoshell-mediated near-infrared thermal therapy of tumors.

- **Drug delivery**

Several studies report the use of gold nanoparticles as a drug delivery vehicle. Tumor necrosis factor-alpha (TNF-α), a cytokine with excellent anticancer activity systemically toxic, which greatly limited its therapeutic effect applications (van Horssen et al 2006; Mocellin and Nitti PEG molar fraction. Importantly, gold nanoparticles with PEG chains of molecular weight (MW) 5000 were internet as efficiently as analogous conjugates with PEG chains of MW 900. Based on this finding, the gold nanoparticles functionalized PEG chains of optimal size (at least z MW 5000 for efficient bypass of RES), with circulation half-life of at least several hours, may be most effective for the treatment of cancer. To make gold nanoparticles more useful for medicine delivery and other biomedical applications (imaging and therapy), must be effective, specific and reliable targeting a specific organ or site of disease without change.Specific in vivo targeting has not been achieved with gold nanoparticle-based drug delivery, given the relatively large total conjugate size (typically greater than 50 nm). diameter) that prohibits efficient extravasation. Although using only passive targeting proved to be effective in some subcutaneous tumor models with xenografts,may not truly reflect the clinical situation. Transgenic and orthotopic tumor models are more clinically relevant and these tumors typically have much less leaky vasculature than subcutaneous which will make passive targeting unsuitable for cancer imaging or therapy. Molecular cancer markers overexpressed on tumor vasculature can be targets of choice.2008). Nanoparticle delivery system consisting of PEG coated gold nanoparticle loaded with TNF-α was constructed maximize tumor damage and minimize systemic TNF-α toxicity (Visaria et al 2006). A combination of local resulted in nanoparticle-based heating and delivery of TNF-α in increased therapeutic efficacy than either treatment alone. Heat-induced delay in tumor growth was enhanced pretreatment with nanoparticles during intravenous administration in the right dosage and timing. It suppresses blood flow from the tumor ion, as well as tumor perfusion defects, suggested vascular damage-mediated killing of tumor cells. Surprisingly the following intravenous administration, little to no accumulation in RES (eg liver and spleen) or other healthy organs animals were observed (Paciotti et al 2004). then this nanoparticle conjugate was also used to det a tumor in an ice ball, again without a significant systetemic toxicity (Goel et al 2007). Phase I clinical trials this conjugate, subsequently named "CYT-6091" (Visaria et al 2007), its safety is currently being evaluated, pharmacokinetics and clinical efficacy.Methotrexate (MTX), a dihydrofolate inhibitor reductase, is a chemotherapeutic agent for the treatment of various types of cancer (Huennekens 1994). MTX-gold nanopartic and cytotoxic/antitumor conjugate was prepd the effect was investigated in vitro and in vivo (Chen et al 2007b).Administration of the conjugate suppressed tumor growth in mouse model of Lewis lung carcinoma, while the same dose of free MTX had no antitumor effect.Nanoshells also tested for drug delivery at specific site. In one early study, composites of hydrogels and gold nanoparticles were developed for photothermally modulated drug delivery (Sershen et al. 2000). Irradiation at 1064 nm was absorbed nanoshells and converted into heat, leading to collapse of the hydrogel, thereby significantly increasing the effect of the drug release. Subsequently, the delivery of the methylene drug is modulated blue, insulin and lysozyme were achieved by irradiation drug-loaded nanoparticle-hydrogel composites with drug release rate dependent on molecular weight therapeutic molecules (Bikram et al 2007). Hollow gold nanoshells can also encapsulate enzymes such as horseradish ish peroxidase (HRP) that remained active inside nanoshell for small but not large substrate molecules (Kumar et al 2005). Not surprisingly, HRP showed none activity when trapped inside solid gold nanoparticles. Drug delivery using gold nanoparticles in combination with their intrinsic ability for photothermal therapy,should be explored in the future. Currently, which type Gold nanoparticles are most suitable for drug delivery of cations is still debatable. It was found that intracellular absorption of different sizes and shapes of gold nanoparticles highly dependent on their physical dimensions

(Chithrani et al 2006). Absorption/scattering efficiency and optical resonance wavelengths were calculated for three commonly used classes of gold nanoparticles: nanospheres, nanoshells and nanorods (Jain et al 2006a). Narrow range in the SPR peaks of the nanospheres (~520-550 nm) led to very limited use for in vivo applications. SPR is peaking gold nanoshells lie favorably in the NIR region. In total extinction of nanoshells has a linear dependence on excess all sizes, but independent of core-to-shell radius ratio. The relative contribution of dispersal to extinction can be is rapidly increased by increasing the size of the nanoshell or decreasing it ratio of the core-to-mantle radius. Gold nanorules were were found to have comparable optical properties at much smaller effective size, with absorption and scattering coefficients orders of magnitude higher than that of nanoshells and nanospheres. While the nanorod with higher aspect ratio and a smaller effective radius is a better photoabsorbing nanoparticket suitable for therapeutic applications that with larger effective radius is preferable for imaging purposes.Studies have shown that femtosecond pulse excitation(at a wavelength of 400 nm) of DNA-modified nanoparticles can lead to desorption of thiolated DNA strands from surface of nanoparticles by breaking the gold-sulfur bond (Jain et al 2006b). This property could be used in the future for controlled drug release. Stability of gold nanoparticles bioconjugates in high ionic strength media acts as a function of nanoparticle size, PEG length, and monolayer composition (Liu et al 2007a). It was found that the stability of the nanoparticles increased with increasing PEG length, decreasing nanoparticle diameter and increasing

Summary

Multifunctionality is a key advantage of nanoparticles over traditional approaches. Targeting ligands, imaging tags, can therapeutic drugs and many other functional groups all be integrated into the nanoparticle conjugate to enable this for targeted molecular imaging and molecular therapy cancer. Gold nanoparticles are unique in their own way interesting optical properties that can be used for both imaging and therapeutic applications. Future of nanomedicine lies in multifunctional nanoplatforms that combine both therapeutic components and multimodality imaging. The ultimate goal is nanoparticle-based substances may enable efficient, specific in vivo drug delivery without systemic toxicity and also the administered dose therapeutic efficacy can be accurately measured without vasively over time. Much remains to be done before that is possible to be a clinical reality and many factors need to be optimized simultaneously for the best clinical outcome. The most promising application of nanoparticles- based funds will be in cardiovascular medicine where there is much less of a biological barrier to effective administration of nanoparticles and in oncology where there is a leaky tumor vasculature may allow better tissue penetration than v normal organs/tissues. We found that quantum dots do after intravenous administration, they do not extravasate from the tumor vasculature injection (Cai et al 2006, 2007a). Since honey nanoparticles are usually much larger than quantum dots (-50 nm vs 25 nm), it is likely that gold nanoparticles do nor extravasative. From photothermal tumor ablation it is only useful when the nanoparticles are large enough (~100 nm in diameter), small gold nanoparticles (10 nm). However, smaller particles may allow for much better extravasation and therefore better tumor targeting efficiency. However, for both large and small gold nanoparticles, vascular targeting may be the only route that exists likely to succeed in the clinic.

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