Available on line www.jocpr.com

Journal of Chemical and Pharmaceutical Research

J. Chem. Pharm. Res., 2010, 2(1): 30-37

ISSN No: 0975-7384

Gold Nanoparticles: A new approach for cancer detection

Parimal M. Prajapati* and Yatri Shah and D J Sen

Department of Pharmaceutical and Medicinal Chemistry, Shri Sarvajanik Pharmacy College, Arvind Baug, Mehsana, Gujarat, India.

Abstract

Gold nanoparticles are produced in a liquid ("liquid chemical methods") by reduction of chloroauric acid ($H[AuCl_4]$), although more advanced and precise methods do exist. Gold nanoparticles are also found to distinguish between cancer cells and noncancerous cells. Another benefit is that the results are instantaneous. “If you take cells from a cancer stricken tissue and spray them with these gold nanoparticles that have this antibody you can see the results immediately. The scattering is so strong that you can detect a single particle. The interaction between light and gold nanostructures is not only useful for the treatment of cancer but also for its diagnosis.

Keywords: Gold nanoparticle ,Colloidal gold, gold nanostructures, Growth Factor Receptor.

Introduction

Colloidal gold, also known as "nanogold", is a suspension (or colloid) of sub-micrometre-sized particles of gold in a fluid — usually water. The liquid is usually either an intense red colour (for particles less than 100 nm), or a dirty yellowish colour (for larger particles). “Gold nanoparticles are very good at scattering and absorbing light,” It has scattering property in a living cell to make cancer detection easier [1-2].

Many cancer cells have a protein, known as Epidermal Growth Factor Receptor (EFGR), all over their surface, while healthy cells typically do not express the protein as strongly. By conjugating, or binding, the gold nanoparticles to an antibody for EFGR, suitably named anti-EFGR. It is able to get the nanoparticles to attach themselves to the cancer cells. “If you add this conjugated

nanoparticle solution to healthy cells and cancerous cells and you look at the image, you can tell with a simple microscope that the whole cancer cell is shining," "The healthy cell doesn't bind to the nanoparticles specifically, so you don't see where the cells are. With this technique, if you see a well defined cell glowing, that's cancer[3-4] ."

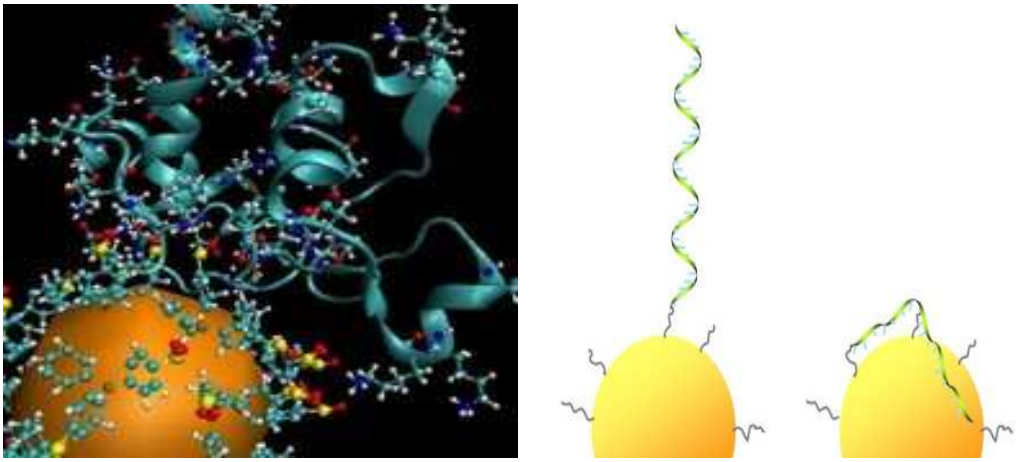

Fig.1 Gold Nanoparticle

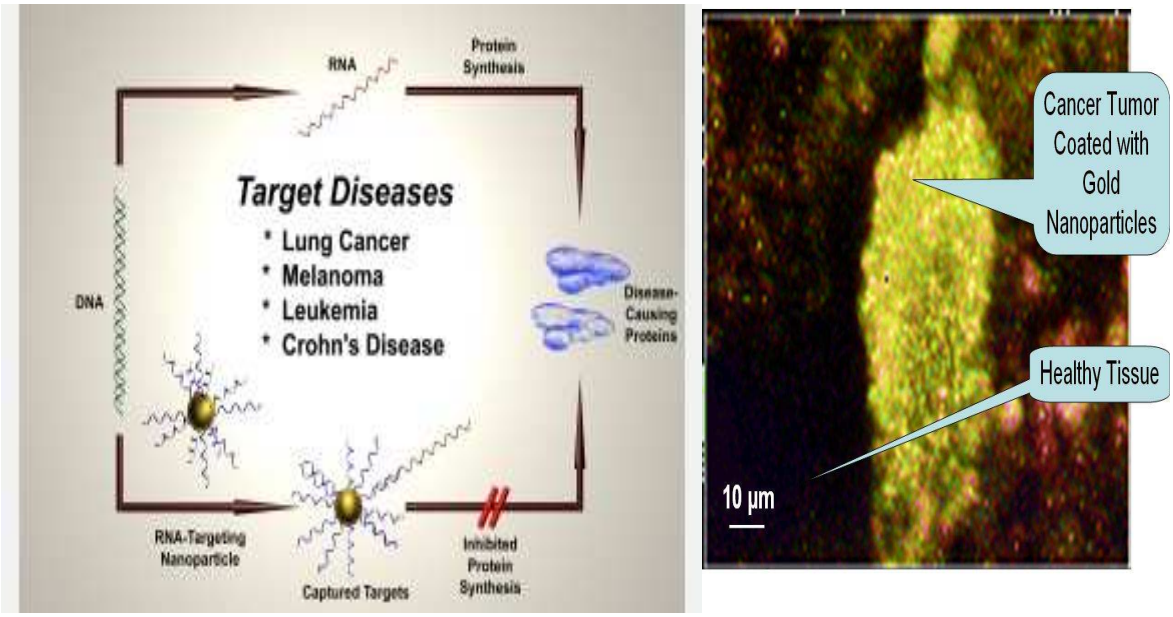

Fig.2 Cancer Tumor Coated With Gold Nanoparticles

The gold nanoparticles have 600 percent greater affinity for cancer cells than for noncancerous cells. The particles that worked the best were 35 nanometers in size. Technique using cell cultures of two different types of oral cancer and one nonmalignant cell line. The shapes of the strong absorption spectrum of the gold nanoparticles are also found to distinguish between cancer cells and noncancerous cells. Another benefit is that the results are instantaneous [5]. "If you take cells from a cancer stricken tissue and spray them with these gold nanoparticles that have this antibody you can see the results immediately. The scattering is so strong that you can detect a single particle," Finally, the technique isn't toxic to human cells. A similar technique using artificial atoms known as Quantum Dots uses semiconductor crystals to mark cancer cells, but the semiconductor material is potentially toxic to the cells and humans. "This technique is very simple and inexpensive to use". It making cancer detection easier, faster and less expensive[6-8]."

Synthesis of gold nanoparticles:

Generally, gold nanoparticles are produced in a liquid ("liquid chemical methods") by reduction of chloroauric acid (H[AuCl4]), although more advanced and precise methods do exist. After dissolving H[AuCl4], the solution is rapidly stirred while a reducing agent is added. This causes Au3+ ions to be reduced to neutral gold atoms. As more and more of these gold atoms form, the solution becomes supersaturated, and gold gradually starts to precipitate in the form of sub-nanometer particles. The rest of the gold atoms that form stick to the existing particles, and, if the solution is stirred vigorously enough, the particles will be fairly uniform in size. To prevent the particles from aggregating, some sort of stabilizing agent that sticks to the nanoparticle surface is usually added. They can be functionalized with various organic ligands to create organic-inorganic hybrids with advanced functionality.It can also be synthesised by laser ablation [9-11].

Fig.3 Steps of Gold Nanoparticles Synthesis

- Add 20 mL of 1.0 mM HAuCl4 to a 50 mL beaker or Erlenmeyer flask on a stirring hot plate. Add a magnetic stir bar and bring the solution just to a boil.
- To the boiling solution, add 2 mL of a 1% solution of trisodium citrate dihydrate, Na3C6H5O7.2H2O. The gold sol gradually forms as the citrate reduces the gold(III). Remove from heat when the solution has turned red. (Gaps in the movie indicate equal gaps in time. The total elapsed time is approximately 10 times the movie length.).
- The presence of a colloidal suspension can be detected by the reflection of a laser beam from the particles [12].

Because a laser pointer emits polarized light, the pointer can be oriented such that the beam appears to disappear. When the beam from the laser is visible in one view, it is invisible in the view perpendicular to the first. Put a small amount of the gold nanoparticle solution in two test tubes. Use one tube as a color reference and add 5-10 drops of NaCl solution to the other tube. Does the color of the solution change as the addition of chloride makes the nanoparticles closer together?

Gold nanoparticles may simplify cancer detection

There are many techniques for cancer diagnosis and treatment, there is still a need for techniques that are more accurate and/or less invasive to the body. The idea is to introduce gold nanoparticles into tumor cells, to which laser light would subsequently be applied. The nanoparticles would heat up to such a degree that the damaged cells would be completely burnt. The interaction between light and gold nanostructures is not only useful for the treatment of cancer but also for its diagnosis.

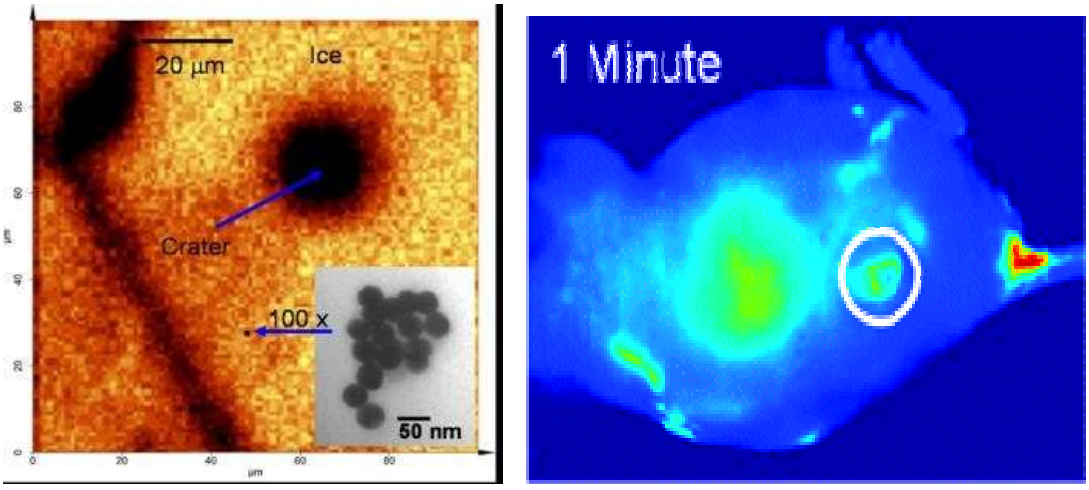

Fig.4 Cancer Detection

Nanoparticles are metal structures that measure just one millionth of a meter: they have a diameter ten thousand times smaller than that of a hair. What is revolutionary about this novel use of nanoparticles is that they can be designed in such a way that they can be selectively introduced into a patient's body so that they only penetrate damaged cells[13-15].
.

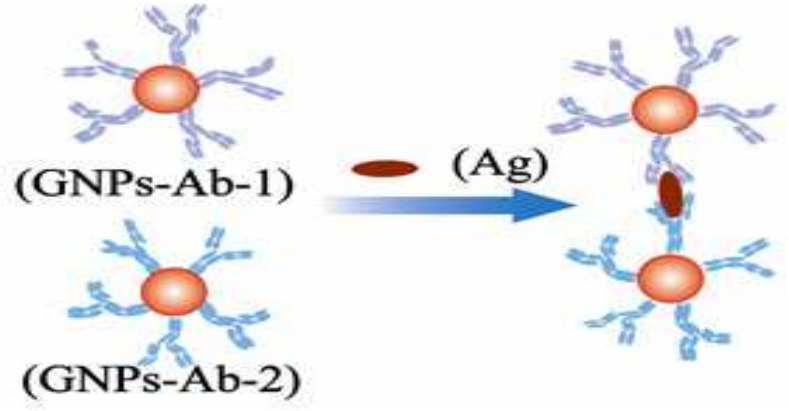

Fig.5 Types of Goldparticles

GNPs-Ab-1 and GNPs-Ab-2 represent the two types of gold nanoparticles bearing different antibodies, and Ag represents the CEA antigen. When mixed, a dimer is formed reducing the total number of nanoparticles in the sample.Thus, the treatment would only affect tumor tissues without damaging healthy ones, as happens with chemotherapy and radiotherapy. **One promising scheme**, which is useful for diagnosis as well as therapy, is to attach gold nanoparticles to tumor cells and illuminate them with infrared laser light. This technique is much less invasive than chemotherapy, X-ray therapy or surgery [16]. Magnetic resonance imaging is noninvasive and capable of detecting cancer tumors when they are very small, but the equipment and its operation are very expensive, meaning that it is often used at a later stage, when the cancer is already more advanced. Ultrasound therapy offers a much cheaper alternative, but the high intensity sound waves that are necessary for treatment cause tissue heating and cavitation (creation of small pockets of gas in the bodily fluids or tissues that expand and contract/collapse). Because of their extremely small size, nanoparticles restrict the motion of electrons in one or more directions. This restriction, called quantum confinement, allows the properties of the particles to be modified by changing their size, in contrast to bulk material whose properties are independent of size. In particular, the properties of the surface become dominant and, in the case of noble metals, resonant electromagnetic radiation will induce large surface electric fields that enhance their radiative properties. This means that the particles absorb much more light than would normally be expected and the light that is not absorbed is scattered much more strongly than expected[17-18]. This absorption and scattering is typically orders of magnitude stronger than the most strongly absorbing molecules and organic dyes. It has been found that gold nanorods and nanocages exhibit strong infrared (IR) absorption and biological compatibility, making them good candidates for use in biological systems. Gold nanorods of different sizes and showed that different aspect ratios between the rod diameter and the length resulted in different absorption spectra. This showed that it is possible to produce biologically compatible nanoparticles with different optical properties. For further investigation, they chose nanoparticles with an aspect ratio of 3.9 because the absorption band overlaps the wavelength at 800 nm, which is the wavelength of a commercial Ti:sapphire laser. Furthermore, this wavelength is in a region where the light extinction of the human tissue is a minimum, resulting in a penetration depth up to 10 cm, which means that almost the whole human body is accessible. Due to their strong scattering, gold nanorods have excellent potential as optical contrast agents for molecular imaging. Furthermore, the strongly absorbed IR radiation can be converted into heat efficiently, making it a promising potential photothermal therapeutic agent. In photothermal

therapy, optical radiation is absorbed and transformed into heat. The heat causes the proteins and DNA to denature, irreversibly damaging the cell and, consequently, causing its death. Usually, photothermal therapy is done with visible light, which is absorbed by the agent as well as the tissue. The use of IR radiation is favourable[19-21].

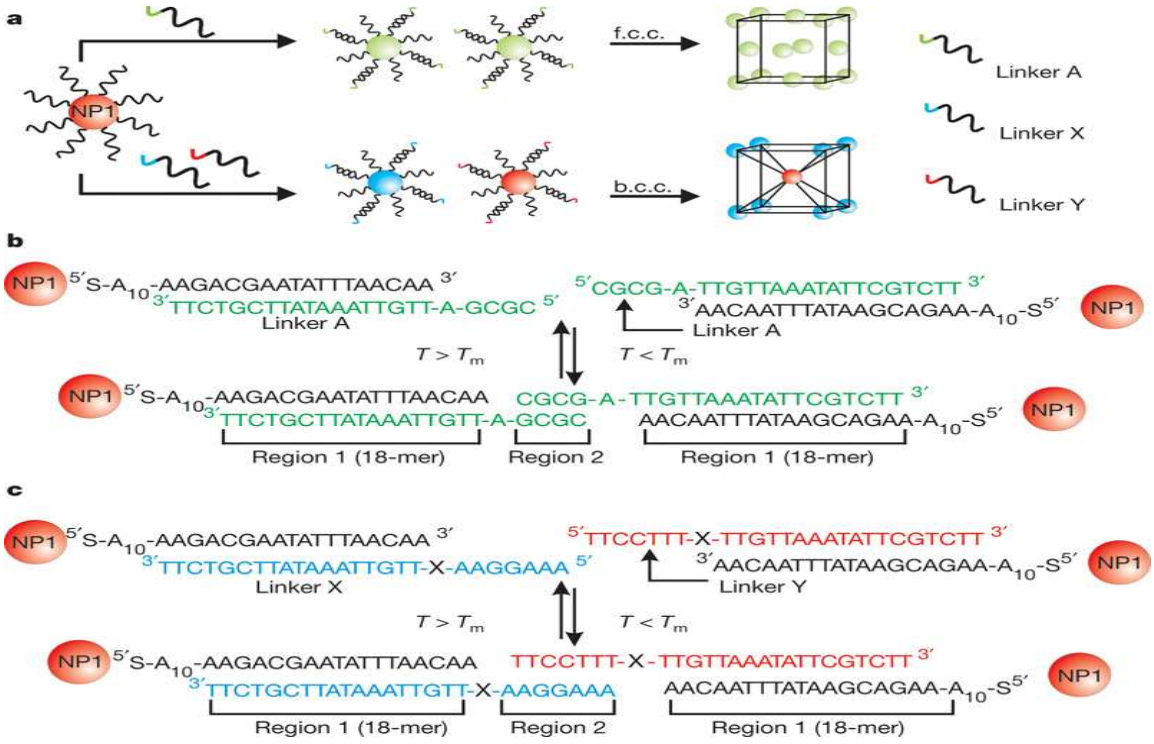

Fig.6 (a), Gold nanoparticle–DNA conjugates can be programmed to assemble into different crystallographic arrangements by changing the sequence of the DNA linkers. (b), Single-component assembly system (f.c.c.) where gold nanoparticles are assembled using one DNA sequence, linker-A. c, Binary-component assembly system (b.c.c.) in which gold nanoparticles are assembled using two different DNA linkers -X and -Y. X in the DNA sequence denotes the flexor region: A, PEG6 or no base. NP1 indicates that the same gold nanoparticle-DNA conjugates were used in all experiments.

Because cell tissue is transparent to IR light, making it possible to diagnose and treat tumor cells deeper in the body. The convenient characteristic bioconjugation (binding to biomolecules) of gold nanostructures improves the target selectivity, so that they can stick to particular proteins, which makes it possible to target cancer cells with the nanoparticles and ensure that unhealthy cells receive most of the energy during therapy. As a result, the photothermal destruction of surrounding healthy tissue is minimized and the damage is much less than that caused during x-ray therapy[22].

Gold nanoparticles may improve antisense cancer therapies:

The potential of antisense DNA therapies for genetic diseases is great, yet the development of antisense DNA-based drugs has been slow. Strands of antisense DNA can bind to complementary messenger RNA (mRNA) transcripts and prevent their translation into proteins. Aantisense DNA which is complementary to mRNA transcripts encoding mutated and disease-causing proteins can prevent production of those proteins and so alleviate disease symptoms [23]. Antisense DNA molecules more stable, and more effective, by attaching them to gold nanoparticles. Attached multiple strands of antisense DNA to individual gold nanoparticles, forming 'antisense nanoparticles' which were inserted into mouse cells engineered to produce green fluorescent protein (GFP). Because the DNA strands used were complementary to the GFP mRNA, their effectiveness could be determined by measuring the amount of fluorescence emitted by the cells. The amount of fluorescence depends on the concentration of GFP in the cell; upon introduction of the nanoparticles, the antisense DNA bound to GFP transcripts, reducing the amount of protein being produced. In consequence, there was a marked dimming in the fluorescence of the cells. The antisense nanoparticles were less toxic, less susceptible to degradation and more readily taken up by cells when compared to antisense DNA complexed with Lipofectamine or Cytofectin (commercially available reagents for introducing DNA into cells). "In the future, this exciting new class of antisense material could be used for the treatment of cancer and other diseases that have a genetic basis," So attached anti-epidermal growth factor receptor (EGF-R) monoclonal antibodies to gold nanoparticles**,** which adhered to cultured cancer cells expressing EGF-R, making them easier to detect [24-25].

Application

Gold nanoparticles has been successfully used as a therapy for,

- Rheumatoid arthritis
- Alzheimer's disease
- The administration of hydrophobic drugs require molecular encapsulation and it is found that nanosized particles are particularly efficient in evading the reticuloendothelial system**.**
- Cancer detection

Conclusion

The gold nanoparticles have 600 percent greater affinity for cancer cells than for noncancerous cells. “This Gold nanoparticle is very simple and inexpensive to use”**.** It makes cancer detection easier, faster and less expensive.” The healthy cell doesn’t bind to the nanoparticles specifically, so you don’t see where the cells are. With this technique, if you see a well defined cell glowing, that’s cancer.”

References

[1] C. N. Ramachandra Rao, Giridhar U. Kulkarni, P. John Thomasa, Peter P. Edwards, *Chem. Soc*. Rev., **2000**, 29, 27-35.

[2] "Colloidal dispersion of gold nanorods: Historical background, optical properties, seed-mediated synthesis, shape separation and self-assembly"**.** *Material Science and Engineering Reports* **65** (1-3): 1–38. **2009**.
[3] J. Turkevich, P. C. Stevenson, J. Hillier, *Discuss Faraday. Soc*. **1951**, 11, 55-75.
[4] J. Kimling, M. Maier, B. Okenve, V. Kotaidis, H. Ballot, A. Plech, *J. Phys. Chem.* B **2006**, 110, 150-157.
[5] G. Frens, *Colloid & Polymer Science* **1972**, 250, 736-741.
[6] G. Frens, *Phys. Sci***. 1973**, 241, 20-22.
[7] BK Pong et al. *J. Phys. Chem.* C, 111 (17), 6281 -6287, **2007**.
[8] M. Brust; M. Walker; D. Bethell; D. J. Schiffrin; R. Whyman (**1994**). *Chem. Commun*... 37 (1):120-134.
[9] Manna, A.; Chen, P.; Akiyama, H.; Wei, T.; Tamada, K.; Knoll, W. (**2003**). *Chem. Mater*. 15 (1): 20–28.
[10] Gay-Lussac (**1832**). *Annalen der Physik* 101 (8): 629–630..
[11] Berzelius, J. J.. *Annalen der Physik* 98 (6): 306–308.
[12] Faraday, M. (**1857**). *Philos. Trans. R. Soc. London* 147: 145.
[13] Zsigmondy, Richard, *Material Science and Engineering Reports* 65 (1-3): 1–38. **2009**.
[14] Jianling Zhang, Jimin Du, Buxing Han, Zhimin Liu, Tao Jiang, Zhaofu Zhang (**2006**). *Angewandte Chemie International Edition* 45: 1116–1119.
[15] Vikas Berry; Ravi F. Saraf (2005). *Angewandte Chemie International Edition* 44 (41): 6668–6673..
[16] Hiroshi Yao; Kanae Miki; Naoki Nishida; Akito Sasaki; Keisaku Kimura (**2005**). *J. Am. Chem. Soc*. 127 (44): 15536 – 15543.
[17] Jacob D. Gibson, Bishnu P. Khanal, and Eugene R. Zubarev *J. Am. Chem. Soc.* **2007**, 129, 11653-11661
[18] Qian, Ximei. *Nature Biotechnology*. **2008**,64,115-134.
[19] S. Mallidi, T. Larson, J. Aaron, K. Sokolov, and S. Emelianov, *Opt. Express* vol. 15, pp. 6583-6588 **2007**.
[20] K. Sokolov, J. Aaron, B. Hsu, D. Nida, A. Gillenwater, M. Follen, C. MacAulay, K. Adler-Storthz, B. Korgel, M. Descour, R. Pasqualini, W. Arap, W. Lam, and R. Richards-Kortum, *Cancer Res. Treat.*, vol. 2, pp. 491-504, **2003**.
[21] J. S. Aaron, N. Nitin, K. Travis, S. Kumar, T. Collier, S. Y. Park, M. José-Yacamán, L. Coghlan, M. Follen, R. Richards-Kortum, and K. V. Sokolov, *J. Biomed. Opt***.**, vol. 12, pp. 034007, **2007**.
[22] M. Follen, J. Aaron, I. Pavlova, A. Malpica, R. Lotan, and R. Richards-Kortum, *Cancer Res*., vol. 63, pp. 1999-2004, 2003.
[23] M. Horisberger, *Scan. Electron Microsc*, vol. 2, pp. 9-31, **1981**.
[24] C. M. Pitsillides, E. K. Joe, X. Wei, R. R. Anderson, and C. P. Lin, *Biophys. J.*, vol. 84, pp. 4023-4032, **2003**.
[25] L. R. Hirsch, R. J. Stafford, J. A. Bankson, S. R. Sershen, B. Rivera, R. E. Price, J. D. Hazle, N. J. Halas, and J. L. West, *Proc. Natl. Acad. Sci. U S A*, vol. 100, pp. 13549-13554, **2003**.