NANO IS A NEW ERA OF MEDICAL HISTORY - A REVIEW

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Summary

Nanotechnology is an emerging field of research and development that seeks new solutions to pressing health and environmental problems by combining physical sciences and engineering with life sciences and medicine. This exciting frontier of discovery is generating new therapies, devices, diagnostic tools, and a better understanding of the relationship between cells and disease. For example, very small devices are now enabling new kinds of minimally invasive medical procedures. Nanobiotechnology represents the future of medicine and healthcare. Advancements in nanobiotechnology are revolutionizing our capability to understand biological intricacies and resolve biological and medical problems by developing subtle biomimetic techniques. Nanocomposites and nanostructured materials are believed to play a vital role of medical field and the future of nano and nanobiotechnology are making a new era in medicinal field.

Keywords: Nanorobots, Magnetic nanoparticles, Alzheimer's disease detection, Carbon nanotubes, Nanowires detect molecular signs of cancer, HIV vaccine.

Introduction

Nanotechnology was originally called onanotechnology, from the persistent habits of its proponents such as Ron Jeremy, but 'o' was later dropped for the decency reasons. The science itself was actually invented in 2073BC by the king of Middle Earth Moses. However, K. Eric Drexler popularized the word nanotechnology in the 1980's period. A nanometer (nm) is one billionth (1x10-9) of a meter, the length of 10 hydrogen atoms placed side by side, or 1/80,000th of the thickness of a human hair. Nanotechnology relates to the organization of atoms and molecules within a size range of 1-100 + nm. The width of a DNA molecule is approximately 2.5 nm. The width of cell membranes ranges over 6-10 nm and the dimensions of protein are in the range 1.0-15.0 or 20 nm.

The Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO 2008) have recognized a need for scientific advice on any food safety implications that may arise from the use of nanotechnologies in the food and agriculture sectors through its horizon scanning activities. With the advent of nanotechnology, the prospects for using medical imaging, disease diagnoses, drug delivery, cancer treatment, gene therapy and other areas have progressed rapidly. The worldwide market for products produced using nanotechnology is estimated to reach US$1 trillion by 2015 (84). Nanobiotechnology represents the convergence of nanotechnology and biotechnology, yielding materials and products that use biological molecules in their construction or are designed to affect biological systems. Several applications of nanobiotechnology include engineering biomolecules for non biological use such as DNA based computer circuits, using nanotechnology tools such as medical diagnostic devices and medical imaging to study biology and combining nanomaterials with biological systems for outcomes such as targeted drug therapies. Nanobiotechnology often studies existing elements of nature in order to fabricate new devices (14). Therefore, the unbridled growth and uses of nanobiotechnology in medical and human health evaluations opens society, and it's could become the asbestos of the 21st century.

Amazing nanoparticle

Nanoparticle utmost use for medical application

Scientists have taken to naming their particles after the real world shapes that they might represent. Nanospheres (1), nanoreefs (20) nanoboxes and more have appeared in the literature. Biological processes that contribute to both health and disease occur at the nanoscale the size scale of proteins, nucleic acids, pores, cellular membranes, and other biomolecules. Patients have actually benefited from the improved efficacy and reduced side effects of nanoparticle based pharmaceuticals since the early 1990s several hundred nanotechnology based products entered US pharmaceutical pipelines in 2006. In addition the beneficial uses of NPs in drug delivery, cancer treatment, and gene therapy may cause unintentional human exposure. Present day nanomedicine exploits carefully structured nanoparticles such as dendrimers (12), carbon fullerenes buckyballs (68) and nanoshells to target specific tissues and organs. These nanoparticles may serve as diagnostic and therapeutic antiviral, antitumor or anticancer agents etc and their effort are given below.

Alzheimer's disease detection

Alzheimer's disease (AD), a brain disorder named for German physician Alois Alzheimer, who first described it in 1906, is a disease that destroys brain cells, causing problems with memory, thinking and behavior. Alzheimer's gets worse over time, and it is fatal. It is also the most common form of dementia. The latest estimate is that 26.6 million people were suffering from Alzheimer's disease worldwide in 2006, and this number will rise to 100 million by 2050 - 1 in 85 of the total population. The latest 2008 data for the US alone estimates that 5 million Americans have the disease, with an estimated increase to 11 to 16 million by 2050. One of the most promising applications of nanoscience is in Alzheimer's disease. As patients can be definitely diagnosed after they pass way and their brain is examined for the telltale damage, scientists are hunting for tests that would help make a diagnosis in living patients.

One possible biomarker for Alzheimer's is a protein called amyloid beta derived diffusible ligands (ADDL). Support for the role of ADDLs comes from their neurotoxicity and presence at elevated levels in the brains of AD patients as compared with the age-matched controls (37). The correlation of CSF ADDL levels with the disease state offers promise for improved AD diagnosis and early treatment. This finding was made possible by combining ADDL-specific monoclonal antibodies (59, 18) with an ultra sensitive, nanoparticle-based protein detection strategy termed biobarcode amplification (BCA) (71). The BCA strategy used by Klein, Mirkin and coworkers (36) makes clever use of nanoparticles as DNA carriers to enable million fold improvements over ELISA sensitivity. CSF is first exposed to monoclonal anti-ADDL antibodies bound to magnetic microparticles. After ADDL binding, the microparticles are separated with a magnetic field and washed before addition of secondary antibodies bound to DNA: Au nanoparticle conjugates. These conjugated to contain covalently bound DNA as well as complementary barcode DNA that is attached via hybridization. UN reacted an antibody: DNA: Au nanoparticle conjugates are removed during second magnetic separation, after which elevated temperature and low salt conditions release the barcode DNA for analysis (55). Because the pathology of AD is thought to begin decades before the first symptoms, it would be very interesting to learn at what stage of disease progression ADDL levels in the CSF rise above those in healthy individuals.

New anticancer therapy

Cancer is an enormous socio-economic problem. According to the National Cancer Institute (NCI), it is estimated that in 2007 there will be over 1.4 million new cases of cancer (of any type) and over 550,000 deaths from cancer in the United States from the American Cancer Society. This makes cancer the second deadliest disease category, after heart diseases. The conventional anti cancer treatments are nonspecific to target killing of tumor cells, may induce severe systemic toxicity, and produce drug resistant phenotypic growth. An exciting potential use of nanotechnology in cancer treatments is the exploration of tumor specific thermal scalpels to heat and burn tumors (73). Observed in mice that selective photo thermal ablation of tumor using near infrared absorbing polyethylene coated gold nanoshells of 130 nm inhibited tumor growth and enhanced survival of animals for up to 90 days compared with controls (80). There further more reported that antibody coated magnetic iron NPs were effective to heat and literally cook the tumors. In similar work performed in athymic mice using an antibody coated iron NPs (23) showed specific targeted binding to tumors and tumor necrosis within 24 hr after therapy with better response. The efficacy of different antibodies conjugated to NPs, including transferring and epidermal growth factor receptor, was examined in animal studies (28). In cancer therapy, enzyme-mediated liposome destabilization and specific phospholipase A2 activation with synergistic membrane perturbing and permeability were reported to be more effective (4). Nanoshells can be used for photo-thermal ablation of tumour (65) tissue as demonstrated both human breast carcinoma cells in vitro and in a murine model in vivo (43). However, electromagnetic interactions between the gold nanoparticles change the property of the metal, making it absorb light from the near infrared, which can easily penetrate several centimeters of (human) tissue without harming it.

In the murine model poly (ethylene glycol)-passivated gold-coated silica nanoshells were injected interstitially ~5 mm into the tumour volume (tumour size 3-5.5 mm). Poly (ethylene glycol) is used to increase circulation time (39) as well as to reduce non specific attachment or uptake (2). The blood vessels inside tumours develop poorly, allowing the nanoshells to leak out and accumulate inside tumors. Six hours after the injections an external laser source of near infrared light (power density ~4-35 W/cm^2) is applied through the skin for 3-7 minutes. The gold nanoparticles readily absorb the energy and turn it into heat resulting in an average temperature increase of ~37 °C which induced irreversible cancerous tissue damage. The heating is localised and does not affect healthy tissue adjacent to the tumour. The mice remain cancer-free after the treatment, whereas growth of tumours in the control group, i.e. no treatment and sham group, continues rapidly. It is also possible to attach biological markers, such as antibodies and proteins, to the nanoshells, in order to direct them to their target tissues (66). The advantage of using smaller particles is that they can be inserted into any part of the human body to treat cancer cells in their infancy.

Hyperthermia can be produced by near-infrared laser irradiation of gold nanoparticles present in tumors and thus induce tumor cell killing via a bystander effect. To be clinically relevant, however, several problems still need to be resolved. In particular, selective delivery and physical targeting of gold nanoparticles to tumor cells are necessary to improve therapeutic selectivity. Considerable progress has been made with respect to retargeting adenoviral vectors for cancer gene therapy. Therefore hypothesized that covalent coupling of gold nanoparticles to retargeted adenoviral vectors would allow selective delivery of the nanoparticles to tumor cells, thus feasibilizing hyperthermia and gene therapy as a combinatorial therapeutic approach. For this, sulfo-N-hydroxysuccinimide labeled gold nanoparticles were reacted to adenoviral vectors encoding a luciferase reporter gene driven by the cytomegalovirus promoter (AdCMVLuc). Covalent coupling could be achieved, while retaining virus infectivity and ability to retarget tumor-associated antigens. These results indicate the possibility of using adenoviral vectors as carriers for gold nanoparticles (29). Development of these new medicines will be a fantastic voyage that we are literally betting our lives on.

Gene therapy

Nanoparticle based gene therapy to be effective in systemic gene treatment of lung cancer using a novel tumor suppressor gene, FUS1 (38). Chitosan a polymer long used in gene therapy was reported to have increased transfection efficiency and decreased cytotoxicity (67). Oral gene delivery in BABL/C mice using poly-L-lysine modified silica NPs has shown success with the distribution of particle throughout the intestinal mucous cell with limited cytoxitycity (63). Recent in vitro work with breast cancer cells has shown the potential efficiency of NP mediated gene delivery of the wild type p53. Cancer cell exposed to these NPs based gene delivery showed an increased and sustained antiproliferative activity not seen in cell exposed to vector alone (81). A nonviral vector for in vivo gene delivery and fluorescent visualization of transfection using organically modified silica NPs has promising success for targeted brain therapy (10). Recently gene therapy against parkinson's disease and this disease is a chronic, progressive disorder of the central nervous system, and is the direct result of the loss of cells in a section of the brain called the substantia nigra.

Those cells produce dopamine, a chemical messenger responsible for transmitting signals within the brain. Loss of dopamine causes critical nerve cells in the brain, or neurons, to fire out of control, leaving patients unable to direct or control their movement in a normal manner. Researchers (University of Kentucky) were recently awarded $66,000 by The Michael J. Fox Foundation for Parkinson's Research (MJFF) under the foundation's Rapid Response Innovation Awards program. They plan to use this technology to transduce brain cells so that they express proteins beneficial to the cell's survival. Test the feasibility of delivering condensed DNA nanoparticles that encode for a neurotrophic factor to the brain as a means to halt or prevent the neurodegenerative process in an animal model of Parkinson's disease. Neurotrophic factors are capable of protecting neurons from dying, thereby rescuing essential neurons in the brain. In animal studies, neurotrophic factors have revived dormant brain cells, caused them to produce dopamine, and prompted dramatic improvement of symptoms. The MJFF Rapid Response Innovation Awards support projects that may have little to no existing preliminary data, but that hold potential to significantly impact understanding or treatment of Parkinson's disease. Developments of these nanoparticles can more effort to treat most complex disease.

HIV vaccine

To improve the immune response against HIV viruses, Baba *et al* (5) developed the vaccine against HIV/AIDS by using a safe antigen carrier, poly (gamma-glutamic acid) nanoparticles. The nanoparticle is biodegradable in human bodies and can bind to the surfaces of various virus protein antigens and can encapsulate those protein antigens into their particles. The study in mice found that poly(gamma-glutamic acid) nanoparticles in the range of 300-400 nm in diameter could bind to the gp120 surface antigen of human immunodeficiency virus type 1 (HIV-1). After the carriers were injected into mice, a strong CD8+ T-cell response to virus protein antigens CD was detected. The stimulation of allogenic T cell proliferation helps to increase the immune system in the body against HIV-1 virus. This lead to the conclusion that poly (gamma glutamic acid) nanoparticles carrying various HIV-1 proteins may be a potential candidate as a novel AIDS vaccine (Baba et al., 2007).

Prevention of telomerase activity

Telomerase, an enzyme that prevents chromosomes from shortening when they divide, is widely suspected of playing a key role in making cancer cells immortal. Chad Mirkin, (Northwestern University) team that developed the new assay (106). The assay system consists of gold nanoparticles coated with short stretches of DNA that can serve as a substrate for telomerase. When a sample containing this enzyme is mixed with these nanoparticles, telomerase binds to the DNA sequences and begins adding repeated stretches of six specific nucleotides to the end of the DNA. After a short time, the investigators wash off any telomerase and then add magnetic microparticles coated with a piece of oligonucleotide that is complementary to the sequence added by telomerase. The coated magnetic microparticles bind to any elongated DNA and enable the researchers to separate those complexes from the rest of the gold nanoparticles by using a magnetic field. Next, the DNA sequences are removed from the gold nanoparticles and are detected using a silver development process and automated reader that Dr. Mirkin's team invented for a related assay system, known as the biobarcode assay.

Using this assay, the investigators were able to reliably detect telomerase activity in as few as 10 to 1,000 tumor cells grown in culture. The researchers then showed that they could detect changes in telomerase activity after the addition of a known inhibitor of the enzyme, suggesting that this assay could help in efforts to develop telomerase inhibitors as anticancer agents.

Magnetic nanoparticles (MNPs) therapy

Magnetic nanoparticles such as super paramagnetic iron oxide nanoparticles (~15 nm in diameter) (50, 49), paramagnetic copper-nickel alloy nanoparticles (~400 nm in diameter) (9), or magnetite (Fe3O4) cationic liposomes (~10-40 nm in diameter) (89, 101, 102) are becoming more and more important for many applications in medical science and data storage technique. In medical applications the magnetic nanoparticles are used for diagnostics and therapy (3). For example, they can serve as a contrast medium in magnetic resonance imaging. There are new potential applications currently under test like drug targeting and hypothermia. The magnetosomes were deposited on a substrate and magnetized vertically before measuring and the stray field of four single particles with a diameter of about 40 nm each. The picture correlates with the picture of vertically magnetized magnetic dipoles. This investigation pointed out that magnetosomes are single domain particles showing a remanent magnetization. The saturation magnetization m and the anisotropy constant k_{eff} of MNP ensembles will be measured using a SQUID susceptometer. The data achieved will serve as input parameters for the analysis and the validation of the MRX data and the demonstrator. The validation is needed to ensure the quality of the data measured using the new equipment in clinical applications and production.

Invigoration of nanorobert in medical field

Nanorobots developed stimulation:

The engineering of molecular products needs to be carried out by robotic devices, which have been termed as nanorobots. A nanorobot is essentially a controllable machine at the nanometer or molecular scale that is composed of nanoscale components. Development of microelectronics in the 1980s has led to new tools for biomedical instrumentation, the manufacturing of nanoelectronics (22), will similarly permit further miniaturization towards integrated medical systems, providing efficient methodologies for pathological prognosis (72, 42). The use of microdevices in surgery and medical treatments is a reality which has brought many improvements in clinical procedures in recent years. More complex molecular machines, or nanorobots, having embedded nanoscopic features represent new tools for medical procedures (31, 76, 69).

Surgical nanorobotics

Surgical nano robots could be introduced into the body through the vascular system or at the ends of catheters into various vessels and other cavities in the human body. A surgical nanorobot, programmed or guided by a human surgeon, could act as a semi autonomous on site surgeon inside the human body. Axotomy of roundworm neurons was performed by femtosecond laser surgery, after which the axons functionally regenerated (103). A femtolaser acts like a pair of nano scissor by vaporizing tissue locally while leaving adjacent tissue unharmed.

Femtolaser surgery has performed for localized nanosurgical ablation of focal adhesions adjoining live mammalian epithelial cells (57), microtubule dissection inside yeast cells (86), noninvasive intratissue nanodissection of plant cell walls and selective destruction of intracellular single plastids or selected parts of them (93), and even the nanosurgery of individual chromosomes (selectively knocking out genomic nanometer sized regions within the nucleus of living Chinese hamster ovary cells). These procedures do not kill the cells upon which the nanosurgery was performed.

Nanorobot for intracranial therapy

Considering the properties of nanorobots to navigate as blood borne devices, they can help on important treatment processes of complex diseases in early diagnosis and smart drug delivery. Their application on different tasks can be performed through embedded nanosensors to identify medical targets inside the human body. Numerical analysis and advanced computational simulation techniques are used to investigate nanorobot interaction and activation for sensing gradient changes of relevant chemical patterns for brain aneurysm. Thus a detailed approach is described serving as a test bed to support the fast development of molecular machines towards new therapies and treatments. An important and interesting aspect in the current development is the fact that, the similar hardware architecture and sensing methodology presented for nanorobots to identify intracranial harmful vessel growth, can also be used for a broad range of problems in medicine, including specialized brain therapies, neurodegenerative problems, and surgery (33). A key factor to increase the changes for patients in having a satisfactory treatment from cerebral aneurysm relies on detection of vessel deformation in early stages of bulbs development.

Assessment of carbon nanotubes and its based sensors

Carbon nanotubes are among the astonishing objects that science sometimes discovers and which will likely revolutionize technological developments of the 21st century. Since carbon nanotube discovery in 1991 by Iijima and carbon nanotubes have been investigated by many researchers all over the world. They can be seen as the nearly one dimensional form of fullerenes. Carbon nanotubes are 100 times stronger than steel, impervious to temperatures up to 6,500 degrees Fahrenheit and only one to a few nanometers in width. Carbon nanotubes arrays can play a key role in the artificial cochlea development (JPL in Pasadena, CA). It has been established that growing of the carbon nanotubes requires use of small metal catalyst particles (~5- 100 nm). Recent discoveries of various forms of carbon nanostructures have stimulated research on their applications in diverse fields. They hold promise for applications in medicine, drug and gene delivery areas (83).

Single walled carbon nanotubes for cancer treatment

Single wall carbon nanotubes having non covalent attachment of various functional groups such as proteins, peptides, enzymes, polysaccharides, porphyrin, DNA, sodium dodecyl sulphonate etc had been synthesized. Owing to their semi conducting properties, single walled carbon nano tubes have been proposed as chemical sensor for gaseous molecule, such as NO_2 or NH_3 (58). Main application of these carbon nano tubes in the therapeutic field is photothermal therapy for cancer. Indeed, although biological systems are transparent to 700-110 nm near infrared (NIR) light, the intrinsic strong absorbance of

single walled carbon nanotubes in this window can be used for optical stimulation of carbon nano tubes inside living cells to afford various useful functions. Kam and his coworkers have shown that this singular property of single walled carbon nanotubes can be used to destroy cancer cells selectively upon irradiation with NIR light (52). This selective cancer cell destruction by appropriately functionalized single walled carbon nanotubes provides new opportunities in the area of cancer therapy. Researchers today have started conducting studies where they use carbon nanotubes as sensors that can locate harmful toxins that damage DNA, as a drug delivery system, and as tools to destroy cancerous cells.

Multiwall carbon nanotube for bone fixations

Multiwall carbon nano tubes are flexible and resilient tubular structure with diameter of 10-40 nanometers, length is 10-150 microns and strength 50-100 times greater than steel at fraction of weight. For the first time, catalytic growth of multiwall carbon nano tubes by CVD was proposed by Yacaman *et al* (99). When Witzmann and Monteiro Riviere analyzed human epidermal keratinocytes (HEKs) exposed to multi walled carbon nanotubes in cell culture using large format of two dimensional (2D) gel electrophoresis and mass spectrometry (MS). Compared with controls, 24 hours of multi walled carbon nanotube exposure altered the expression of 36 proteins ($P < 01$), whereas 106 were altered at 48 hours. At both time points, roughly 67% of the affected proteins were significantly down regulated. Peptide mass fingerprinting identified most of the differentially expressed proteins, and the various protein identities reflected a complex cellular response to multi walled carbon nanotube exposure. In addition to proteins associated with metabolism, cell signaling, and stress, they observed a consistent effect on the expression of cytoskeletal elements and vesicular trafficking components. These data clearly show that multi walled carbon nanotubes are capable of altering protein expression in a target epithelial cell that constitutes a primary route of occupational exposure for manufactured nanotubes (97). The addition of multiwall carbon nanotubes improved the fatigue performance of acrylic bone cement by as much as seven times. As the bone cement was loaded, the multiwall carbon nanotubes resisted the separation of the crack faces. Although it is unlikely that one carbon nanotube could provide enough resistance to slow the growth of the crack, it is likely that thousands of carbon nanotubes, working in parallel, can greatly slow the rate of crack growth. The cumulative effects of crack bridging, therefore, were slower crack growth and increased fatigue life. These findings suggest that the addition of multiwall carbon nanotubes is a promising solution to the problem of fatigue failure.

Japanese scientists (Shinshu University School of Health Sciences in Matsumoto, Japan) tested highly crystalline multiwall carbon nanotubes with an average diameter of 80 nm and a length from 10 to 20 μm, prepared by catalytic chemical vapor deposition and subsequent thermal treatment above 2800°C in argon. To examine their influence on bone healing, the researchers implanted 100 nanoliters of multiwall carbon nanotubes in defects (0.7 mm in diameter and 2 mm deep) created in the shin-bones of mice. After four weeks, they found that the cortical bone and the bone marrow cavity were completely restored. Observation of the interface between the multiwall carbon nanotube particles and bone matrix disclosed that multiwall carbon nanotubes adhered directly to the bone itself.

For the third issue, new bone formation, the scientists used bone morphogenetic proteins (BMPs), a group of proteins known for their ability to induce the formation of bone and cartilage. They made a composite consisting of BMP, multiwall carbon nanotubes and collagen, and implanted it in the dorsal musculature of mice. Again they found that multiwall carbon nanotube particles were integrated entirely into new bone and bone marrow, but also that, in comparision to a control group using only BMP/collagen, the multiwall carbon nanotubes seemed to accelerate new bone formation in response to BMP. Further more it finally confirmed that hydroxyapatite was formed and crystallized on the multiwall carbon nanotube surface in simulated body fluid remarkably quickly, and that the multiwall carbon nanotubes acted as the core for the initial hydroxyapatite crystallization. The results of these experiments demonstrate that multiwall carbon nanotubes possess good bone compatibility, as indicated by the minimal inflammatory reaction. Their results thus indicate the compatibility of multiwall carbon nanotubes with biomaterials positioned in contact with bone and their suitability for use in regions of bone healing such as fracture sites and finding should facilitate development of new drug delivery systems or scaffold materials for bone regeneration using multiwall carbon nanotubes. Furthermore, including multiwall carbon nanotubes in implants for the treatment of fractures, such as plates and screws, may promote bone repair and thus facilitate rapid fracture healing. As is true generally safety-related testing involving carcinogenesis and other toxicity is necessary prior to carbon nanotube use in humans.

Monitoring blood glucose

Carbon nanotubes are promising to sense candidates to monitor glucose in blood and urine. Multiwall carbon nanotubes as well as singlewall carbon nanotubes have been used to develop enzymatic amperometric biosensors (51, 91, 94) or fluorimetric biosensors (8). The enzyme glucose oxidase is either immobilised inside multiwall carbon nanotubes or non-covalently attached to the surface of singlewall carbon nanotubes enabling the catalysis of glucose with hydrogen peroxide as co-product. For the amperometric biosensor, the enzyme immobilization allows for the direct electron transfer from the enzyme to a gold or platinum transducer producing the response current. The fluorescence biosensor could be used in a new type of implantable biological sensor such as near-infrared nanoscale sensor. This sensor could be inserted into tissue, excited with a laser pointer, and provide real-time, continuous monitoring of blood glucose levels. It consists of protein encapsulated singlewall carbon nanotubes functionalized with potassium ferrocyanide, a substance that is sensitive to hydrogen peroxide. The ferrocyanide ion adsorbs on the surface through the porous monolayer. When present, hydrogen peroxide will form a complex with the ion, which changes the electron density of the carbon nanotube and consequently, its optical properties. The more glucose that is present, the brighter the carbon nanotube will fluoresce. The sensor can be loaded into a porous capillary and inserted into tissue. As carbon nanotubes do not degrade like organic molecules that fluoresce, these nanoparticle optical sensors would be suitable for long-term monitoring applications. Proof-of-concept studies to detect glucose levels have been performed in vitro, i.e. in blood samples. Practical use is five to ten years ahead, according to the researchers. Self-assembled peptide nanotubes can be used in an electrochemical biosensor (104). The presence of the peptide nanotubes improves the sensitivity of the device several fold.

Peptide nanotubes offer several advantages over carbon nanotubes, since they are biocompatible, water-soluble, inexpensive, easy to manufacture, and can be chemically modified by targeting their amino or carboxyl groups. The sensing technique can be used as a platform for ultra-sensitive detection of biological and chemical agents.

Capnography and detect disease

Carbon nanotube-based chemical gas sensors have great potential in medical applications. Currently, Nanomix Inc. (Emeryville, California, USA) is developing a medical capnography sensor using polyethylene-imine-coated carbon nanotubes. Capnography is the measurement of carbon dioxide concentration in human respiration and is an indicator of patient status during administration of anaesthesia. The tiny, low power sensor will be the first disposable electronic capnography sensor and has the potential to extend the reach of quantitative respiratory monitoring beyond the operating room and into ambulatory and emergency settings as well as doctors' offices. Various applications have been reported illustrating the broad potential of carbon nanotube based biosensors, such as biosensing platforms for the simultaneous detection of dopamine and ascorbic acid for the diagnosis of Parkinson's disease (48, 96), and dopamine and serotonin (98), and a nitric oxide radical biosensor (95). Recently, a more generalized approach for enzyme-based biosensors has been demonstrated by immobilising enzymes in redox hydrogels incorporating singlewall carbon nanotubes (Joshi et al., 2005).the invigoration of nanotube and based sensor detect disease is will given long lives to people.

Protein transporters

Many therapeutic agents may turn out to be proteins, but proteins can be difficult to get across the cell membrane and into the cytoplasm while still retaining their biological function. Singlewall carbon nanotubes could become a new class of a generic tool for delivering small peptides (75) and proteins (53) into cells in vitro as well as in vivo. Acid-oxidised singlewall carbon nanotubes bind various types of proteins (≤80 kD) and transport them through the cell membrane. These acids treated carbon nanotubes are stable in water and do not aggregate, as do untreated carbon nanotubes. The uptake mechanism is not fully understood and proposed mechanisms are endocytosis (54), phagocytosis (19), and insertion and diffusion through the lipid bilayer of the cell membrane (11). In many instances, a cell breaks down proteins transported via endocytosis, but the singlewall carbon nanotube bound proteins avoid this fate if concurrently a small amount of the antimalarial drug chloroquine is delivered leading to swelling of the endosomal compartments and eventual rupture (74). For reasons that are still unclear, acid-treated carbon nanotubes are able to bind a large protein, human immunoglobulin (~150 kD), but are not able to transport that protein across the cell membrane. To test if carbon nanotubes can deliver small proteins that then retain their biological activity once inside the cell, singlewall carbon nanotubes were used to deliver the protein cytochrome c (cyt-c) which triggers apoptosis. Cell line experiments showed that singlewall carbon nanotube bound cyt-c retained its biological activity and did cause significantly higher rates of apoptosis than did either cyt-c or the nanotubes alone. Whether cyt-c remains attached to the nanotubes or whether it is released into the cytoplasm has to be elucidated and these were unambiguously help to medicinal fields.

Sniff out lung cancer

Hossam Haick, and his colleagues at the Israel Institute of Technology in Haifa, used a network of 10 sets of chemically modified carbon nanotubes to create a multicomponent sensor capable of discriminating between a healthy breath and one characteristic of lung cancer patients (79). Meanwhile, Silvano Dragonieri, M.D., Italy, and his colleagues used a commercial nanoarray-based electronic nose to be discriminating between the breath of patients with non-small cell lung cancer and chronic obstructive pulmonary disease (COPD) (27). The key development in Dr. Haick's team's work demonstrated that the electrical resistance of carbon nanotubes coated with nonpolymeric organic layers changes substantially when nonpolar organic molecules, such as those present in a breath, pass over the nanotubes. Uncoated nanotubes do not respond strongly to the type of nonpolar molecules found in the human breath. Using 10 different organic coatings, the investigators created field effect transistors comprising random networks of each of the different coated nanotubes, and the resulting array produces a characteristic change in electrical output when exposed to volatile nonpolar organic substances. A computational technique known as principal component analysis can decipher the complex signal change produced when mixtures of nonpolar organic molecules pass over the sensor network. When plotted in two dimensions, the data from a simulated set of healthy and lung cancer patients from two clear clusters that readily distinguish the two sets of patients. The investigators also showed that their device could identify healthy rats from those with chronic kidney failure. Rather than designing their own device, Dr. Dragonieri's group used a Cyranose 320 built by Smiths Detection based in Pasadena, California. This hand-held electronic nose, which is used widely throughout the chemical and food processing industries, employs a nanocomposite sensor array to rapidly detect volatile organic compounds in the air. In this study, Dr. Dragonieri's team collected breath samples from 10 patients with NSCLC, 10 with COPD, and 10 healthy controls. After drying the samples, the investigators analyzed them using the Cyranose 320 and its onboard statistical software. Smellprints, analogous to fingerprints, from the three groups of patients were clearly distinguishable, with no ambiguity among the three groups. The investigators note that these results warrant conducting a large-scale, prospective clinical trial to determine whether this system could be useful in real clinical settings, including physician offices.

Quantum dots medical breakthrough

Quantum dots are spherical nano sized crystals. They can be made of nearly every semiconductor metal (e.g., CdS, CdSe, CdTe, ZnS, PbS), but alloys and other metals (e.g. Au) can also be used (6, 107). The prototypical quantum dot is cadmium selenide (CdSe). Quantum dots range between 2 and 10 nm in diameter (10 to 50 atoms). In the early 1990s, quantum dots were mainly prepared in aqueous solution with added stabilizing agents. This procedure yielded low quality quantum dots with poor fluorescence efficiencies and large size variations. From 1993 onwards, the high-temperature organometallic procedure was used for growing quantum dots (70). Biomedical monitoring applications have taken considerable advantage of using quantum dots for sensitive optical imaging in fixed cells and tissues, living cells and animal models. In addition, quantum dots can be conjugated to biological molecules such as proteins, oligonucleids, small molecules, etc. which are used to direct binding of the quantum dots to areas of interest for biolabelling and biosensing (15).

Quantum dots (Qdots) are now used extensively for labeling in biomedical research (17), and this use is predicted to grow because of their many advantages over alternative labeling methods. Moreover, quantum dots have brighter emission and good photostability.

In vivo tumour targeting and imaging

Targeted molecular imaging of tumours was first demonstrated in nude mice using quantum dots (34). Nude mice lack a thymus and a functional immune system. Therefore, a human xenograft of tumour cells will be accepted and grow in nude mice. This xenograft tumour model is therefore an excellent model to study in vivo targeting of therapeutics to human cancer cells. Moreover, the vasculature of most cancer tissue is highly disordered, causing exposed interstitial tissue, so that tumour antigens are in direct contact with blood. Nude mice with human prostate tumours were injected intravenously with poly (ethylene glycol)-conjugated quantum dots functionalised with anti bodies against the prostate specific membrane antigen. The permeability and retention effect is due to the inherent vasculature permeability of the microenvironment of cancerous tissue, combined with the lack of lymphatic drainage. Due to the permeability and retention effect alone, it was found that nonconjugated poly (ethylene glycol) quantum dots accumulated in induced mouse tumours, demonstrating tumour contrast, but much less efficiently than actively targeted probes. Recently, an intraoperative highly sensitive technique for pulmonary sentinel lymph node mapping using near-infrared fluorescent quantum dots has been developed (90). The study showed the feasibility of the technique for mapping pulmonary lymphatic drainage and guiding excision of the sentinel lymph node in a porcine model. In addition, the application of quantum dots in multiphoton intravital microscopy shows great versatility for studying tumour pathophysiology (92). Intravital microscopy is a powerful imaging technique that allows continuous non-invasive monitoring of molecular and cellular processes in intact living tissue with 1-10 μm resolution (47). Quantum dots can be customized to concurrently image and differentiate tumour vessels from both perivascular cells and matrix and to monitor the trafficking of bone marrow-derived precursor cells to the tumour vasculature allowing to investigate the degree to which the vascular and perivascular structures are formed or remodelled in response to cell homing.

Deliver SiRNA Therapy

Take a quantum dot, add a coating of poly(ethylene glycol) (PEG), and attach a homing peptide and a piece of small interfering RNA (siRNA), and the result is a targeted nanoparticle that can stop the production of a specific protein by a targeted cell. If the homing peptide targets tumor cells and the siRNA molecule shuts down a cancer-related protein. The investigators chose a commercially available, PEG-coated quantum dot that passes easily through skin and other tissues. The PEG coating renders the quantum dots biocompatible and provides an attachment site for the homing peptide and siRNA. However, the small size of the quantum dot and the chemical makeup of PEG result in only about 100 total attachment sites for both the homing peptide and siRNA molecule. In addition two types of linkers for attaching siRNA molecules one permanent but flexible, the other capable of releasing free siRNA once the nanoparticle is taken into the targeted cell. After conducting exhaustive studies of particle uptake and siRNA release and determined that a ratio of 20 homing peptides to 1 siRNA molecule produced the

optimal level of protein suppression (24). These studies also demonstrated the superiority of using a cleavable linkage for attaching the siRNA molecule. The result could be a new type of anticancer agent that would also double as an imaging agent.

Treat common cause of blindness

Emerging nanotechnologies have a great potential to uncover the cause of cataract and may provide a good solution for its treatment. The lens is comprised of tightly packed epithelial cells and lens fibers, enclosed in a thin capsule although the lens fibers have few organelles and their protein content is very high. The lens consists of 35% protein and 65% water. In addition, there are three classes of proteins in the human lens. The researchers (University of Ulster) used intact porcine lenses from five-month-old pigs, intact human lenses obtained from three donors aged 41, 42 and 45 years, and sections of human lens cortex obtained from four donors aged 11, 19, 32, and 34 years were incubated for 72 hours at 7°C in aqueous solutions of green (566 nm) and red (652 nm) fluorescent water soluble cadmium tellurium (CdTe) nanoparticles. They were able to demonstrate that CdTe quantum dots diffused into the lens capsule and the cortical lens fibers but did not pass through the intact lens capsule. Since dextan, which has a diameter at least twice that of the nanoparticles can passively diffuse through the lens capsule, the negative charge, carboxyl group, and/or the alkaline pH of the nanoparticles may have prevented the nanoparticles from passing through the capsule. Future studies are required to determine the critical variables necessary for the diffusion of nanoparticles through the lens capsule and these researches reveal that fluorescent nanoparticles used to enhance visualization of the lens capsule during cataract surgery (87).

Multiple Disease Markers

The use of antibodies linked to quantum dots, in combination with a technique known as multispectral imaging, to detect 11 Cluster of Differentiation markers in fixed human lymphoid tissue samples. The researchers (National Institutes of Health, USA) attached quantum dots with unique emission spectra the color of light they emit when irradiated with light to each of 11 commercially available antibodies that target these differentiation markers. Mainly streptavidin conjugated quantum dots with distinct emission spectra were tested for their utility in identifying a variety of differentially expressed antigens (surface, cytoplasmic, and nuclear). Slides were analyzed using confocal laser scanning microscopy, which enabled with a single excitation wavelength (488 nm argon laser) the detection of up to seven signals (streptavidin-conjugated quantum dots 525, 565, 585, 605, 655, 705 and 805 nm) plus the detection of 4'6-DiAmidino 2 PhenylIndole with an infra-red laser tuned to 760 nm for two photon excitation. Each of these signals was specific for the intended morphologic immunohistochemical target. In addition, five of the seven streptavidin conjugated quantum dots tested (not streptavidin-conjugated quantum dots 585 or 805 nm) were used on the same tissue section and could be analyzed simultaneously on routinely processed formalin-fixed, paraffin-embedded sections. Application of this multiplexing method will enable investigators to explore the clinically relevant multidimensional cellular interactions that underlie diseases, simultaneously and the development of multi-target quantum dot-based diagnostic systems there are still many factors that need to be examined to optimize the use of these nanoscale beacons (30).

Detecting Cell Death

Researchers (University of Maastricht, Netherlands) have developed a nanoparticle that can spot apoptosis, using both MRI and fluorescence imaging. Animals test showed that this nanoparticle can provide anatomical information using MRI and cellular level information using fluorescence imaging. Imaging programmed cell death in the body could provide an early indication that an antitumor therapy is indeed killing cancer cells. Importantly biocompatible molecular structure capable of binding strongly to eight gadolinium atoms, and then linked multiple carriers to each fluorescent quantum dot and also attached one molecule of annexin A5 (82). The resulting nanoparticle contained enough gadolinium atoms to produce a strong MRI signal that would be detectable even if only a few of the nanoparticles were able to bind to an apoptotic cell. To test the imaging ability of this nanoparticle, the investigators added it to cells triggered to start apoptosis. During the initial stages of apoptosis, the researchers were able to detect small patches of green fluorescence on the cell membrane. As apoptosis continued, these green patches spread across the entire cell membrane. MRI experiments showed that the nanoparticle produced an imaging signal that was approximately 40 times stronger than that produced by the gadolinium carrier alone. Subsequent imaging experiments were able to detect injury induced apoptosis in mice.

Important nanowires

Nanowires can be synthesized using a large variety of materials such as metals, e.g. Ag (13), semimetals, e.g. Bi (105), semiconductors, e.g. CdS (85), and superconductors, e.g. Zn (62). Silicon nanowire field-effect transistor devices have been used as pH sensors (21). Photocurrent response to UV light irradiation suggests that ZnO nanowires could be a good candidate for optoelectronic switches (56). Nanowires have also been proposed for use in inorganic-organic solar cells (45) and multifunctional of this nanowire bioscaffolds on titanium (26). In addition, nanoscale light-emitting diodes with colours ranging from the ultraviolet to near-infrared region could be combined with microfluidics in lab-on-a-chip systems to produce highly integrated analytic systems that might enable applications ranging from high-throughput screening to medical diagnostics to be developed (44).

Nanowires detecting individual viruses

Semiconducting silicon nanowires can be configured as field-effect transistors for the electrical detection of viruses in solutions (77). When a single charged virus binds to receptors (e.g., antibodies) linked to the nanodevice the conductance of a semiconducting nanowire changes from the baseline value, and when the virus unbinds, the conductance returns to the baseline value. The conductance of a second nanowire device without receptors should show no change during the same time period and can serve as an internal control. Nanowires are confined to a central region that is coupled to a microfluidic channel for sample delivery and the conductance response can be recorded while solutions with viruses flow at a constant rate. Modification of different nanowires within an array with receptors specific for different viruses provides a means for simultaneous detection of multiple viruses at the single particle level. The potential of nanowire-based electrical detection of viruses exceeds the capabilities of other methods such as polymerase chain reaction-based assays (35) and micromechanical devices (40).

Harvard University scientists have found that ultra thin silicon wires can be used to electrically detect the presence of single viruses, in real time, with near perfect selectivity (http://nanotechwire.com/news.asp?nid=1138) and the silicon wires can be configured as ultra sensitive detectors that turn on or off in the presence of a single virus. Mainly, they're used merged nanowires conducting a small current with antibody receptors for certain key domains of viruses such as agglutinin in the influenza A virus. When an individual virus came into contact with a receptor, it sparked a momentary, telltale change in conductance that gave a clear indication of the virus's presence. In addition to influenza A, their groups tested nanowire arrays outfitted with receptors specific to paramyxo virus and adenovirus and the detectors could differentiate among the three viruses both because of the specific receptors used to snag them because each virus binds to its receptor for a characteristic length of time before dislodging leaving only a minuscule risk of a false positive reading. Finally, the researchers said that any anti bioterror device built around nanowires virus detecting capabilities would most likely marry the technology with a micro fluidic apparatus that would draw in air, suspend any airborne particles in a liquid, and then run this solution past the nanowire array (64).

Polymer nanowires detect cancer biomarker

Investigators at the University of California have developed a simple and cost-effective method of building conducting polymer nanowires that can detect a wide range of levels of a cancer biomarker (7). Ashok Mulchandani, research team developed a new device. At its heart lies polypyrrole nanowires connected to a pair of gold electrodes spaced a mere 3 microns apart and also use an applied electric field to move individual nanowires into proper alignment on the gold electrodes. They then coat the nanowires with a material known as EDC that can serve as an attachment point for antibodies and other molecules that bind to specific cancer biomarkers. The investigators attached an antibody that binds to the cancer biomarker CA 125. When solutions with known concentrations of CA 125 were applied to the biosensor, the device accurately measured concentrations as low as 1 enzymatic unit per milliliter (U/mL) of solution to as high as 1,000 U/mL. The maximal normal blood level of CA 125 is considered to be 35 U/mL. The researchers obtained identical results when they tested human blood plasma for CA 125 levels. The researchers note that their next step will be to create a device capable of measuring a panel of disease markers simultaneously. They also plan to incorporate their biosensor into a microfluidic device that would be suitable for use in a portable disease detection system.

Spectrum of nanotech new curative value

Antidiabetic effect

Permanent solution for diabetic patients could be artificial pancreas. The original idea was first described in 1974. The concept of its work is simple, a sensor electrode repeatedly measures the level of blood glucose; (http://www.sciencedirect.com/science?ob= Article) this information feeds into a small computer that energizes an infusion pump, and the needed units of insulin enter the bloodstream from a small reservoir (41). However, the main problem and the reason why most patients refused to have such an artificial organ was its size. Today, it is logical to assume that nanotechnology can solve the problem. An American company, Medtronic MiniMed, has been working on a device

called Long Term Sensor System (LTSS), which links an implantable long-term glucose mini sensor with an implantable insulin mini pump. The main problem is how to develop and refine a sophisticated algorithm to translate glucose levels determined by the sensor into appropriate insulin dosages. Testing of the LTSS to date is promising and MiniMed scientists predict they can bring an artificial pancreas to market by the year 2008. It is not hard to imagine what the artificial pancreas might bring to diabetes patients. Ideally, it would mean nearly normal glycemia, no checking of blood glucose levels, no risk of hyper/hypoglycemia, no (or very few) chronic diabetic complications, no chronic immunosuppression as in islet transplantation, etc. There is no doubt that with its small size, artificial pancreas would be an acceptable solution for every diabetic patient. Another one great alternative for pancreatic tissue transplantation could be so called an artificial beta cell. The cells can be genetically altered so that they could not only produce insulin, but could also respond to the rise and fall of blood glucose, just as normal pancreatic beta cells do (25). Illani Atwater, Ph.D., from Sansum Medical Research Institute, Santa Barbara, CA, is working on inserting the proinsulin gene into a keratinocyte cell line attached to a glucose sensitive promoter gene, (http://www.childrenwithdiabetes.com/_on_701.htm) as well as the genes for GLUT2 glucose transporters and glucokinase phosphorylation enzymes. No matter which way leads toward the solution, the result will be the same, i.e. artificial beta cell that will produce insulin in response to the rise of blood glucose, and no target for the immune system. Medical applications of cantilever-based sensors have been proposed for early diagnosis of diabetes mellitus (60) and can improve blood glucose monitoring using small and ultra-sensitive analytical platforms (78, 100). In patients with diabetes mellitus, ketones are produced due to the deterioration of blood insulin concentrations. Acetone is one of these ketones which is excreted in urine or expired as vapour in exhaled air. Disposable test kits are used to detect acetone in urine. Acetone in exhaled air can only be detected by the physician as a putrid smell without any quantification. Small amounts of acetone in a patient's breath can be detected by cantilever array sensor technique which may attribute to early diagnosis of diabetes mellitus.

Detects bacteria

The Centers for Disease Control and Prevention (CDC) keep some pretty scary statistics and estimated that foodborne pathogens cause approximately 76 million illnesses, 325,000 hospitalizations, and 5,000 deaths in the United States each year. Researchers have created a nanowell device to identify bacteria. A group of researchers at Texas A&M University has developed a nanotechnology to rapidly detect and identify bacteria. The researchers call their technique 'SEnsing of Phage-Triggered Ion Cascade', or SEPTIC. The SEPTIC technique uses bacteriophages viruses that attack bacteria. When a bacteriophage infects a bacterium, it punctures the wall of the cell in order to inject its genetic material. As a result, ions leak out of the host cell (about 100 million in total). This causes tiny fluctuations in the electric field around the bacterium. The scientists use an extremely small container (a nanowell) and tiny electrodes to detect these microscopic electric-field fluctuations. The key to specificity comes from the properties of the phage: they are very choosy about which bacteria they infect. The researchers tested the technique on three strains of E. coli bacteria, using three different phages. They had a 100 per cent success rate in detecting and identifying the bacteria. Nanorods also highly detect bacteria such as *Salmonella, Listeria,* and *Toxoplasma* these pathogens are

responsible for 1,500 deaths each year. *Salmonella* is the most common cause of foodborne deaths and responsible for millions of cases of foodborne illness a year. The research team at the University of Georgia fabricated a hetero-structured silicon/gold nanorod array by the glancing angle deposition thin film method and functionalized it with anti-*Salmonella* antibodies and organic dye molecules. Due to the high aspect ratio nature of the silicon nanorods, dye molecules attached to the silicon nanorods produce an enhanced fluorescence upon capture and detection of *Salmonella* (32). In their experiment, they managed to capture a single *Salmonella* bacterium with the antibodies conjugated on the gold and detected by thousands of dye molecules immobilized on the silicon nanorods. In principle, the protocol developed in this study could be used for detecting other foodborne pathogenic bacteria such as *E.coli*, *Staphylococcus*, *Campylobacter* and food toxins such as Ricin, Abrin, or Clostridium Botulinum if the proper antibody is selected for the conjugation with nanorod substrates. Additionally, the fluorescent detection dye can also be replaced by other types of dyes or potentially quantum dots that may allow for multiplex detection.

Rapidly detect viruses

Respiratory syncytial virus (RSV) sends about 120,000 children to the hospital in the United States each year. Although it is only life-threatening in one case out of every 100, it infects virtually all children by the time they are five. Few children in the U.S. die from RSV, but it also attacks the elderly, causing some 17,000 to 18,000 deaths annually. Nanotechnology diagnostic tests that can detect rapidly viruses as diverse as human papillomavirus (HPV), influenza, and respiratory syncytial virus (RSV) in as little as 60 seconds (88). A research teams at the University of Georgia describes its new technique based on surface enhanced Raman scattering (SERS). SERS works by measuring the change in frequency of a near-infrared laser as it scatters off viral DNA or RNA. After experimenting with several different metals and methods, the investigators found that they could amplify a SERS signal from viral DNA using rows of silver nanorods deposited on a glass slide and, like someone positioning a TV antenna to get the best reception, they tried several angles until they found that the signal is best amplified when the nanorods are arranged at an 86-degree angle. The researchers have shown that the technique works with viruses isolated from infected cells grown in a lab, and the next step is to study its use in biological samples such as blood, feces, or nasal swabs. Technician could readily reference a Raman shift for a particular virus to identify an unknown virus. Presently, viruses are first diagnosed with methods that detect the antibodies this person produces in response to an infection. The tests are also prone to false negatives because some people don't produce high levels of antibodies. Taking a different approach, they used fluorescent organic nanocrystals to detect viral DNA amplified using polymerase chain reaction (PCR) (16) and report that using these organic nanocrystals produces as much as a 147-fold increase in the sensitivity of standard PCR assays for HPV, the virus that causes cervical cancer. To prepare the nanocrystals, the investigators mixed a common fluorescent dye with a water soluble polymer for three days. The researchers then coated the nanoparticles with the molecule streptavidin, which forms a tight molecular coupling with a second molecule, biotin. The researchers took advantage of this coupling by incorporating biotin into the DNA molecules produced during PCR amplification of HPV DNA using a well established protocol.

After completing PCR amplification, the investigators simply added the organic nanocrystals and measured the resulting fluorescent signal, which was directly proportional to the amount of HPV DNA present in a sample. However, viruses in human blood samples, such as HIV-1, can be detected using nanoscale antibody array-based devices (61). Dip pen nanolithography was used to pattern 16-mercaptohexadecanoic acid into an array of 60 nm dots on a gold thin film. Monoclonal antibodies to the HIV-1 p24 antigen were immobilised on the dots. The analysis consists of immersing the array for one hour in a blood plasma sample. Subsequently, the signal from the antigen-array binding was amplified using gold nanoparticles probes functionalised with polyclonal antibodies in a solution for one more hour. A measurable amount of HIV-1 p24 antigen in blood plasma from humans with less than 50 copies of RNA/ml is feasible demonstrating that nano based assays can far exceed the 5 pg/ml (pico (p) = 10-12) detection limit of conventional enzyme-linked immunosorbent assays and provide sensitivity comparable to a polymerase chain reaction based assay, without target amplification. Nanobased array biodetection could enable HIV-1 diagnosis in mother-to-child transmission. The nanoelectromechanical systems device with molecular also recognition for virus particle detection has been developed, allowing improvement of the detection sensitivity up to 6 bound baculovirus particles (46). Once these devices with on-chip antibody-based recognition are integrated with sample concentrators, nanomechanical oscillators may prove to present available strategy for ultra-sensitive detection of airborne bacteria, fungi, and virus particles.

Conclusion

Nanotechnology offers important new tools expected to have a great impact on many areas in medical technology. It provides extraordinary opportunities to improve materials and medical devices and they contain several chemical, physical, engineering and biological sciences. When the nanometer scale partial arrangement of molecular component with in living cell gives enormous spectrum of emergent properties, including itself and convergence of these fields now exciting new possibilities for using nanostructure and intelligent nanoscale device to improve human health and hence to open a new era of nanomedicine. In particular, relevant applications are reported in surgery, cancer diagnosis and therapy, biodetection of disease markers, molecular imaging, implant technology, tissue engineering, and devices for drug, protein, gene, and radionuclide delivery. The future that can be envisioned for improvements in public health through the application of nanotechnologies, including nanomedicine and nanobiotechnology seems bright and these discoveries already are revolutionizing manufacturing processes of many material and devices that find broad application in society.

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References

1. Agam MA, Guo Q. Electron beam modification of polymer nanospheres. Journal of Nanoscience and Nanotechnology. 2007. 7: 3615-3619.
2. Akerman ME, Chan WC, Laakkonen P, Bhatia SN, Ruoslahti E. Nanocrystal targeting in vivo. Proc.Natl. Acad. Sci. USA. 2002. 99:12617-12621.
3. Albrecht M, Janke V, Sievers S, Siegner U, Schuler D, Heyen U. Scanning force microscopy study of biogenic nanoparticles for medical applications. J. Magn. Magn. Mat. 2005. 290-291, 269-271.
4. Andresen TL, Davidsen J, Begtrup M, Mouritsen OG, Jorgensen K. Enzymatic release of antitumor ether lipids by specific phospholipase A2 activation of liposome forming prodrugs. J Med Chem. 2004. 47: 1694-1703.
5. Baba M, Wang X, Uto T, Akagi T, Akashi M. An approach to protein based anti AIDS vaccines using biodegradable nanoparticles. Research for Evolutional Science and Technology (CREST), Japan Science and Technology Agency (JST), Tokyo, Japan, May 01. 2007.
6. Bailey RE, Nie S. Alloyed semiconductor quantum dots: Tuning the optical properties without changing the particle size. J. Am. Chem. Soc. 2003.125: 7100-7106.
7. Bangar MA, Shirale DJ, Chen W, Myung NV, Mulchandani A. Single Conducting Polymer Nanowire Chemiresistive Label-Free Immunosensor for Cancer Biomarker. Anal. Chem. 2009. 8: 2168–2175.
8. Barone PW, Baik S, Heller DA, Strano MS. Near-infrared optical sensors based on single-walled carbon nanotubes. Nature Mater. 2004. 4: 86-92.
9. Bettge M, Chatterjee J, Haik Y. Physically synthesized Ni-Cu nanoparticles for magnetic hyperthermia. Biomagn. Res. Technol. 2004. 2: 4-9.
10. Bharali DJ, Klejbor I, Stachowiak EK, Dutta P, Roy I, Kaur N. Organically modified silica nanoparticles: a nonviral vector for in vivo gene delivery and expression in the brain. Proc Natl Acad Sci U.S.A. 2005. 102: 11539-11544.
11. Bianco A, Hoebeke J, Godefroy S, Chaloin O, Pantarotto D, Briand JP, Muller S, Partidos CD, Prato M. Cationic carbon nanotubes bind to CpG oligodeoxynucleotides and enhance their immunostimulatory properties. J. Am. Chem. Soc. 2005. 127: 58-59.
12. Borges AR, Schengrund CL. Dendrimers and antivirals: a review. Curr Drug Targets Infect Disord. 2005. 5: 247-254.
13. Braun E, Eichen Y, Sivan U, Ben-Yoseph G. DNA-templated assembly and electrode attachment of a conducting silver wire. Nature. 1998. 391: 775-778.
14. Brooks BR, Bruccoleri RE, Olafson BD, States DJ, Swaminathan S, Karplus M A. Program for macromolecular energy, minimization, and dynamics calculations. J Comp Chem. 1983. 4: 187-217.
15. Bruchez M, Moronne M, Gin P, Weiss S, Alivisatos AP. Semiconductor nanocrystals as fluorescent biological labels. Science. 1998. 281: 2013-2016.
16. Chan CP, Tzang LC, Sin K, Ji S, Cheung K, Tam T, Yang MM, Renneberg R, Seydack M Biofunctional organic nanocrystals for quantitative detection of pathogen deoxyribonucleic acid. Analytica Chimica Acta. 2007. 584: 7-11.
17. Chan WC, Nie S. Quantum dot bioconjugates for ultrasensitive nonisotopic detection. Science. 1998. 281: 2016-2018.

18. Chang L, Bakhos L, Wang Z, Venton DL, Klein WL. J. Mol. Neurosci. 2003. 20: 305-313.
19. Cherukuri P, Bachilo SM, Litovsky SH, Weisman RB. Near-infrared fluorescence microscopy of single-walled carbon nanotubes in phagocytic cells. J. Am. Chem. Soc. 2004.126: 15638-15639.
20. Choy JH, Jang ES, Won JH, Chung JH, Jang DJ, Kim YW. Hydrothermal route to ZnO nanocoral reefs and nanofibers. Appl. Phys. Lett. 2004. 84: 287.
21. Cui Y, Lieber CM. Functional nanoscale electronic devices assembled using silicon nanowire building blocks. Science. 2001. 291: 851-853.
22. Das S, Gates AJ, Abdu HA, Rose GS, Picconatto CA, Ellenbogen JC. Designs for ultra-tiny, special-purpose nanoelectronic circuits. IEEE Transaction on Circuits and Systems I Regular Paper. 2007. 54: 2528-2540.
23. DeNardo SJ, DeNardo GL, Miers LA, Natarajan A, Foreman AR, Gruettner C. Development of tumor targeting bio-probes (111In-chimeric L6 monoclonal antibody nanoparticles) for alternating magnetic field cancer therapy. Clin Cancer Res. 2005.11: 7087-7092.
24. Derfus AM, Chen AA, Min DH, Rouslahti E, Bhatia SN. Targeted quantum dot conjugates for siRNA delivery. Bioconjug Chem. 2007.18:1391-1396.
25. Dinsmoor RS. Islet cell transplantation. Working towards a cure. Electronic resource. 2006. available at http://www.childrenwithdiabetes.com/_on_701.htm.
26. Dong W, Zhang T, Epstein J, Cooney L, Wang H, Li Y, Jiang YB, Cogbill A, Varadan V, Tian ZR. Multifunctional Nanowire Bioscaffolds on Titanium. Chem. Mater. 2007. 19: 4454–4459.
27. Dragonieri S, Annema J, Schot R, van der Schee M, Spanevello A, Carratu P, Resta O, Rabe K, Sterk P. An electronic nose in the discrimination of patients with non small cell lung cancer and COPD. Lung Cancer. 2009. 64: 166-170.
28. El-Sayed IH, Huang X, El-Sayed MA. Selective laser photo-thermal therapy of epithelial carcinoma using anti-EGFR antibody conjugated gold nanoparticles. Cancer Lett. 2006. 239:129-135.
29. Everts M, Saini V, Leddon J L, Kok R J, Stoff-Khalili M, Preuss M A, Millican C L, Perkins G, Brown J M, Bagaria H, Nikles D E, Johnson D T, Zharov V P, Curiel D T. Covalently Linked Au Nanoparticles to a Viral Vector: Potential for Combined Photothermal and Gene Cancer Therapy. Nano Lett. 2006. 6: 587-591.
30. Fountaine TJ, Wincovitch SM, Geho DH, Garfield SH, Pittalunga S. Multispectral imaging of clinically relevant cellular targets in tonsil and lymphoid tissue using semiconductor quantum dots. Mod Pathol. 2006.19: 1181-1191.
31. Freitas RA. Nanotechnology, Nanomedicine and Nanosurgery. International Journal of Surgery. 2005. 3: 1-4.
32. Fu J, Park B, Siragusa G, Jones L, Tripp R, Zhao Y, Cho Y. An Au/Si hetero-nanorod-based biosensor for *Salmonella* detection. Nanotechnology. 2008. 19: 1-7.
33. Gao Q, Wolfgang MJ, Neschen S, Morino K, Horvath TL, Shulman GI, Fu X Y. Disruption of neural signal transducer and activator of transcription 3 causes obesity, diabetes, infertility, and thermal dysregulation. Proc. Natl. Acad. Sci. U.S.A. 2004.101: 4661- 4666.
34. Gao X, Cui Y, Levenson RM, Chung LW, Nie S. In vivo cancer targeting and imaging with semiconductor quantum dots. Nature Biotechnol. 2004. 22: 969-976.

35. Gardner SN, Kuczmarski TA, Vitalis EA, Slezak TR. Limitations of TaqMan PCR for detecting divergent viral pathogens illustrated by hepatitis A, B, C, and E viruses and human immunodeficiency virus. J. Clin. Microbiol. 2003. 41: 2417-2427.
36. Georganopoulou DG, Chang L, Nam JM, Thaxton CS, Mufson EJ, Klein WL, Mirkin CA. Assessment of CSF levels of tau protein in mildly demented patients with Alzheimer's disease. Proc. Natl. Acad. Sci. U.S.A. 2005.102: 2273-2276.
37. Gong Y, Chang L, Viola KL, Lacor PN, Lambert MP, Finch CE, Krafft GA, Klein WL. Proc. Nat. Acad. Sci. U.S.A. 2003. 100: 10417-10422.
38. Gopalan B, Ito I, Branch CD, Stephens C, Roth JA, Ramesh R. Nanoparticle based systemic gene therapy for lung cancer: molecular mechanisms and strategies to suppress nano-particle-mediated inflammatory response. *Technol* Cancer Res Treat. 2004. 3: 647-657.
39. Gref R, Minamitake Y, Peracchia MT, Trubetskoy V, Torchilin V, Langer R. Biodegradable longcirculating polymeric nanospheres. Science. 1994. 263: 1600-1603.
40. Gupta A, Akin D, Bashir R. Single virus particle mass detection using microresonators with nanoscale thickness. Appl. Phys. Lett. 2004. 84: 1976-1978.
41. Hanazaki K, Nose Y. Brunicardi FCh. Artificial endocrine pancreas. J Am Coll Surg. 2006. available at http://www.sciencedirect.com/science?_ob=Article
42. Hede S, Huilgol N. Nano: the new nemesis of cancer. J. Cancer Res. Ther. 2006. 2: 186-195.
43. Hirsch LR, Stafford RJ, Bankson JA, Sershen SR, Rivera B, Price RE, Hazle JD, Halas NJ, West JL. Nanoshell-mediated near-infrared thermal therapy of tumors under magnetic resonance guidance. Proc. Natl.Acad. Sci. USA 2003. 100: 13549-13554.
44. Huang Y, Duan X, Lieber CM. Nanowires for integrated multicolor nanophotonics. Small. 2005.1:142- 147.
45. Huynh WU, Dittmer JJ, Alivisatos AP. Hybrid nanorod-polymer solar cells. Science. 2002. 295: 2425-2427.
46. Ilic B, Yang Y, Craighead HG. Virus detection using nanoelectromechanical devices. Appl. Phys. Lett. 2004b. 85: 2604-2606.
47. Jain RK, Munn LL, Fukumura D. Dissecting tumour pathophysiology using intravital microscopy. Nature Reviews Cancer. 2002. 2: 266-276.
48. Jiang L, Liu C, Jiang L, Peng Z, Lu G. A chitosan-multiwall carbon nanotube modified electrode for simultaneous detection of dopamine and ascorbic acid. Anal. Sci. 2004. 20: 1055-1059.
49. Jordan A, Scholz R, Maier-Hauff K, Johannsen M, Wust P, Nadobny J, Schirra H, Schmidt H, Deger S, Loening S. Presentation of a new magnetic field therapy system for the treatment of human solid tumors with magnetic fluid hyperthermia. J. Magnetism Magn. Mater. 2001. 225: 118-126.
50. Jordan A, Scholz R, Wust P, Fähling H, Roland F. Magnetic fluid hyperthermia (MFH): Cancer treatment with AC magnetic field induced excitation of biocompatible superparamagnetic nanoparticles. J.Magnetism Magn. Mater. 1999. 201: 413-419.

51. Joshi PP, Merchant SA, Wang Y, Schmidtke DW. Amperometric biosensors based on redox polymer-carbon nanotube-enzyme composites. Anal. Chem. 2005. 77: 3183-3188.
52. Kam NW, O'Connell M, Wisdom JA, Dai H. Carbon nanotube as multifunctional biological transporters and near infrared agent for selective cancer cell destruction. Proc. Natl. Acad. Sci. U.S.A. 2005. 102: 11600-11605.
53. Kam NWS, Dai H. Carbon nanotubes as intracellular protein transporters: Generality and biological functionality. J. Am. Chem. Soc. 2005. 127: 6021-6026.
54. Kam NWS, Jessop TC, Wender PA, Dai H. Nanotube molecular transporters: Internalization of carbon nanotube-protein conjugates into mammalian cells. J. Am. Chem. Soc. 2004.126: 6850-6851.
55. Keating CD. Nanoscience enables ultrasensitive detection of Alzheimer's biomarker. PNAS. 2005. 7: 2263-2264.
56. Kind H, Yan H, Messer B, Law M, Yang P. Nanowire ultraviolet photodetectors and optical switches. Adv. Mater. 2002.14: 158-160.
57. Kohli V, Elezzabi AY, Acker JP. Cell nanosurgery using ultrashort (femtosecond) laser pulses: applications to membrane surgery and cell isolation. Lasers Surg Med. 2005. 37: 227-230.
58. Kong J, Franklin NR, Zhou C. Nanotube molecular wires as chemical sensors. Science. 2000. 287: 622-625.
59. Lambert M P, Viola KL, Chromy BA, Chang L, Morgan TE, Yu J., Venton DL, Krafft G. A, Finch CE, Klein WL. Vaccination with soluble Abeta oligomers generates toxicity neutralizing antibodies. J. Neurochem. 2001. 79: 595-605.
60. Lang HP, Hegner M, Meyer E, Gerber CH. Nanomechanics from atomic resolution to molecularrecognition based on atomic force microscopy technology. Nanotechnology. 2002. 13: 29-36.
61. Lee KB, Kim EY, Mirkin CA, Wolinsky SM. The use of nanoarrays for highly sensitive and selective detection of human immunodeficiency virus type 1 in plasma. Nano Lett. 2004. 4: 1869-1872.
62. Li Y, Cheng GS, Zhang LD. Fabrication of highly ordered ZnO nanowire arrays in anodic alumina membranes. J. Mater. Res. 2000. 15: 2305-2308.
63. Li Z, Zhu S, Gan K, Zhang Q, Zeng Z, Zhou Y. Poly-l-lysine-modified silica nanoparticles: a potential oral gene delivery system. J Nanosci Nanotechno. 2005. 5: 1199-1203.
64. Lieber CM, Patolsky F, Zheng G, Hayden O, Lakadamyali V, Zhuang X. Harvard scientists find nanowires capable of detecting individual viruses. Biomedicine. September 22. 2004. available at. http://nanotechwire.com/news.asp?nid=1138.
65. Loo C, Lin A, Hirsch L, Lee MH, Barton J, Halas N, West J, Drezek R. Nanoshell-enabledphotonics-based imaging and therapy of cancer. Technol. Cancer Res. Treat. 2004. 3: 33-40.
66. Loo C, Lowery A, Halas N, West J, Drezek R. Immunotargeted nanoshells for integrated cancer imaging and therapy. Nano Lett. 2005. 5: 709-711.
67. Mansouri S, Cuie Y, Winnik F, Shi Q, Lavigne P, Benderdour M. Characterization of folate-chitosan-DNA nano-particles for gene therapy. Biomaterials. 2006. 27: 2060-2065.

68. Mashino T, Shimotohno K, Ikegami N, Nishikawa D, Okuda K, Takahashi K. Human immunodeficiency virus-reverse transcriptase inhibition and hepatitis C virus RNA-dependent RNA polymerase inhibition activities of fullerene derivatives. Bioorg Med Chem Lett. 2005.15: 1107-1109.
69. Murphy D, Challacombe B, Khan MS, Dasgupta P. Robotic technology in urology. Postgrad. Med. J. 2006. 82: 743-747.
70. Murray CB, Norris DJ, Bawendi MG. Synthesis and characterization of nearly monodisperse CdE (E = S, Se, Te) semiconductor nanocrystallites. J. Am. Chem. Soc. 1993.115: 8706-8715.
71. Nam JM, Thaxton CS, Mirkin CA. nanoparticle based bio-bar codes for the ultra sensitive detection of proteins. Science. 2003. 301: 1884-1886.
72. Narayan RJ, Kumta PN, Sfeir C, Lee DH, Olton D, Choi D. Nanostructured ceramics in medical devices: applications and prospects. JOM. 2004.56: 38-43.
73. O'Neal DP, Hirsch LR, Halas NJ, Payne JD, West JL. Photo thermal tumor ablation in mice using near infrared-absorbing nanoparticles. Cancer Lett. 2004. 209:171-176.
74. Ogris M, Steinlein P, Kursa M, Mechtler K, Kircheis R, Wagner E. The size of DNA/transferrin-PEI complexes is an important factor for gene expression in cultured cells. Gene Ther. 1998. 5: 1425-1433.
75. Pantarotto D, Briand JP, Prato M, Bianco A. Translocation of bioactive peptides across cell membranes by carbon nanotubes. Chem. Commun. Camb. 2004a. 1: 16-17.
76. Patel GM, Patel GC, Patel RB, Patel JK, Patel M. Nanorobot: a versatile tool in nanomedicine. J. Drug Target. 2006. 14: 63-67.
77. Patolsky F, Zheng G, Hayden O, Lakadamyali M, Zhuang X, Lieber CM. Electrical detection of single viruses. Proc. Natl. Acad. Sci. USA. 2004. 101: 14017-14022.
78. Pei J, Tian F, Thundat T. Glucose biosensor based on the microcantilever. Anal. Chem. 2004.76: 292-297.
79. Peng G, Tisch U, Haick H. Detection of Nonpolar Molecules by Means of Carrier Scattering in Random Networks of Carbon Nanotubes: Toward Diagnosis of Diseases via Breath Samples. Nano Lett. 2009. 9: 1362–1368.
80. Perkel JM. The ups and downs of nanobiotech. The Scientist. 2004.18: 14-18.
81. Prabha S, Labhasetwar V. Nanoparticle-mediated wild-type p53 gene delivery results in sustained antiproliferative activity in breast cancer cells. Mol Pharmacol. 2004.1: 211-219.
82. Prinzen L, Miserus R J J H M, Dirksen A, Hackeng T M, Deckers N, Bitsch N J, Megens R T T A, Douma K, Heemskerk J W, Kooi M E, Frederik PM, Slaaf DW, Zandvoort M A M J, Reutelingsperger C P M. Optical and Magnetic Resonance Imaging of Cell Death and Platelet Activation Using Annexin A5-Functionalized Quantum Dots. Nano Lett. 2007. 7: 93-100.
83. Rao C N R, Cheetham A K. Science and technology of nanomaterials: current status and future prospects. Journal of Materials Chemistry. 2001. 11: 2887-2894.
84. Roco MC. Environmentally responsible development of nanotechnology. Environ Sci Technol. 2005. 39: 106-112.

85. Routkevitch D, Bigioni T, Moskovits M, Xu JM. Electrochemical fabrication of CdS nanowire arrays in porous anodic aluminum oxide templates. J. Phys. Chem. 1996. 100: 14037-14047.
86. Sacconi L, Tolic Norrelykke IM, Antolini R, Pavone FS. Combined intracellular three dimensional imaging and selective nanosurgery by a nonlinear microscope. J Biomed. 2005.10: 14002.
87. Schachar R A, Chen W, Woo B K, Pierscionek B K, Zhang X, Ma L. Diffusion of nanoparticles into the capsule and cortex of a crystalline lens. Nanotechnology. 2008.19: 025102.
88. Shanmukh S, Jones L, Driskell J, Zhao Y, Dluhy R, Tripp RA. Rapid and Sensitive Detection of Respiratory Virus Molecular Signatures Using a Silver Nanorod Array SERS Substrate. Nano Lett. 2006. 6: 2630-2636.
89. Shinkai M, Yanase M, Honda H, Wakabayashi T, Yoshida J, Kobayashi T. Intracellular hyperthermia for cancer using magnetite cationic liposomes: In vitro study. Jpn. J. Cancer Res. 1996. 87: 1179-1183.
90. Soltesz EG, Kim S, Laurence RG, DeGrand AM, Parungo CP, Dor DM, Cohn LH, Bawendi MG, Frangioni JV, Mihaljevic T. Intraoperative sentinel lymph node mapping of the lung using near-infrared fluorescent quantum dots. Ann. Thorac. Surg. 2005. 79: 269-277.
91. Sotiropoulou S, Chaniotakis NA. Carbon nanotube array-based biosensor. Anal. Bioanal. Chem. 2003. 375: 103-105.
92. Stroh M, Zimmer JP, Duda DG, Levchenko TS, Cohen KS, Brown EB, Scadden DT, Torchilin VP, Bawendi MG, Fukumura D, Jain RK. Quantum dots spectrally distinguish multiple species within the tumor milieu in vivo. Nature Med. 2005.11: 678-682.
93. Tirlapur UK, Konig K. Femtosecond near infrared laser pulses as a versatile non invasive tool for intra tissue nanoprocessing in plants without compromising viability. Plant J. 2002.31: 365-374.
94. Wang SG, Zhang Q, Wang R, Yoon SF. A novel multi-walled carbon nanotube-based biosensor for glucose detection. Biochem. Biophys. Res. Commun. 2003. 311: 572-576.
95. Wang Y, Li Q, Hu S. A multiwall carbon nanotubes film-modified carbon fiber ultramicroelectrode for the determination of nitric oxide radical in liver mitochondria. Bioelectrochemistry. 2005c. 65: 135-142.
96. Wang Z, Liu J, Liang Q, Wang Y, Luo G. Carbon nanotube-modified electrodes for the simultaneous determination of dopamine and ascorbic acid. Analyst. 2002b. 127: 653-658.
97. Witzmann FA, Monteiro-Riviere NA. Multi walled carbon nanotube exposure alters protein expression in human keratinocytes. Nanomedicine: Nanotechnology, Biology, and Medicine. 2006. 2: 158-168.
98. Wu K, Fei J, Hu S. Simultaneous determination of dopamine and serotonin on a glassy carbon electrode coated with a film of carbon nanotubes. Anal. Biochem. 2003a. 318: 100-106.

99. Yacaman M J, Yoshida M M, Rendon L, Santiesteban JG. Catalytic growth of carbon microtubules with fullerene structure. Appl. Phys. Lett. 1993. 62: 202-204.
100. Yan X, Ji HF, Lvov, Y. Modification of microcantilevers using layer-by-layer nanoassembly film forglucose measurement. Chem. Phys. Lett. 2004. 396: 34-37.
101. Yanase M, Shinkai M, Honda H, Wakabayashi T, Yoshida J, Kobayashi T. Intracellular hyperthermia for cancer using magnetite cationic liposomes: Ex vivo study. Jpn. J. Cancer Res. 1997. 88: 630-632.
102. Yanase M, Shinkai M, Honda H, Wakabayashi T, Yoshida J, Kobayashi T. Intracellular hyperthermia for cancer using magnetite cationic liposomes: An in vivo study. Jpn. J. Cancer Res. 1998. 89: 463-469.
103. Yanik MF, Cinar H, Cinar HN, Chisholm AD, Jin Y, Ben Yakar A. Neurosurgery: functional regeneration after laser axotomy. Nature. 2004. 432: 822.
104. Yemini M, Reches M, Rishpon J, Gazit E. Novel electrochemical biosensing platform using selfassembled peptide nanotubes. Nano Lett. 2005. 5: 183-186.
105. Zhang Z, Ying JY, Dresselhaus MS. Bismuth quantum-wire arrays fabricated by a vacuum melting and pressure injection process. J. Mater. Res. 1998.13: 1748.
106. Zheng G, Weston L, Daniel and Mirkin C A. A New Approach to Amplified Telomerase Detection with Polyvalent Oligonucleotide Nanoparticle Conjugates. J. Am. Chem. Soc. 2008.130: 9644–9645.
107. Zheng J, Zhang C, Dickson RM. Highly fluorescent, water-soluble, size-tunable gold quantum dots. Phys. Rev. Lett. 2004a. 93: 077402.