

CANCER: A NANOTECHNOLOGICAL APPROACHES**Vaya Raj Kumar^{*}, Modi Ketul, Vaya Rajesh and Shirsat K. Mrunal**

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ABSTRACT

Cancer is not a single disease. It is a group of more than 200 different diseases. The current decades are marked not by the development of new molecules for the cure of various diseases but rather the development of new delivery methods for optimum treatment outcome. Nanomedicine is perhaps playing the biggest role in this concern. Nanomedicine offers numerous advantages over conventional drug delivery approaches and is particularly the hot topic in anticancer research. Nanoparticles (NPs) have many unique criteria that enable them to be incorporated in anticancer therapy. This paper is an overview of advances and prospectus in application of nanotechnology for cancer prevention, detection and treatment. It is addressed how nanotechnology can help solve one of the most challenging and

longstanding problem in medicine, which is how to eliminate cancer without harming normal body tissue.

KEYWORDS: Cancer, Nanotechnology, Nanopartical, Drug Delivery.

INTRODUCTION

There is no one definition that describes all cancers. They are a large family of diseases which form a subset of neoplasms, which show some features that suggest of malignancy. A neoplasm or tumor is a group of cells that have undergone unregulated growth, and will often form a mass or lump, but may be distributed diffusely.

The cancer may also spread to more distant parts of the body through the lymphatic system or bloodstream. Not all tumors are cancerous; benign tumors do not invade

neighboring tissues and do not spread throughout the body. There are over 200 different known cancers that affect humans.

The causes of cancer are diverse, complex, and only partially understood. Many things are known to increase the risk of cancer, including tobacco use, dietary factors, certain infections, exposure to radiation, lack of physical activity, obesity, and environmental pollutants. These factors can directly damage genes or combine with existing genetic faults within cells to cause cancerous mutations. Approximately 5–10% of cancers can be traced directly to inherited genetic defects. Many cancers could be prevented by avoid smoking, eating more vegetables, fruits and whole grains, eating less meat and refined carbohydrates, maintaining a healthy weight, exercising, minimizing sunlight exposure, and being vaccinated against some infectious diseases.^[1]

Six characteristics of malignancies have been proposed:

1. Sustaining proliferative signaling,
2. Evading growth suppressors,
3. Resisting cell death,
4. Enabling replicative immortality,
5. Inducing angiogenesis, and
6. Activating invasion and metastasis.

The progression from normal cells to cells that can form a discernible mass to outright cancer involves multiple steps.^[2]

Signs and Symptoms

When cancer begins it invariably produces no symptoms with signs and symptoms only appearing as the mass continues to grow or ulcerates. Cancer is the new "great imitator". Thus it is not uncommon for people diagnosed with cancer to have been treated for other diseases to which it was assumed their symptoms were due.^[1-2]



1. Local effects

Local symptoms may occur due to the mass of the tumor or its ulceration. For example, mass effects from lung cancer can cause blockage of the bronchus resulting in cough or pneumonia; esophageal cancer can cause narrowing of the esophagus, making it difficult or painful to swallow; and colorectal cancer may lead to narrowing or blockages in the bowel, resulting in changes in bowel habits. Masses in breasts or testicles may be easily felt. Ulceration can cause bleeding which, if it occurs in the lung, will lead to coughing up blood, in the bowels to anemia or rectal bleeding, in the bladder to blood in the urine, and in the uterus to vaginal bleeding. Although localized pain may occur in advanced cancer, the initial swelling is usually painless. Some cancers can cause build up of fluid within the chest or abdomen.

2. Systemic Symptoms

General symptoms occur due to distant effects of the cancer that are not related to direct or metastatic spread. These may include: unintentional weight loss, fever, being excessively tired, and changes to the skin. Hodgkin disease, leukemias, and cancers of the liver or kidney can cause a persistent fever of unknown origin. Specific constellations of systemic symptoms, termed paraneoplastic phenomena, may occur with some cancers. Examples include the appearance of myasthenia gravis in thymoma and clubbing in lung cancer.

3. Metastasis

Symptoms of metastasis are due to the spread of cancer to other locations in the body. They can include enlarged lymph nodes, hepatomegaly or splenomegaly which can be felt in the abdomen, pain or fracture of affected bones, and neurological symptoms. Most cancer deaths are due to cancer that has spread from its primary site to other organs (metastasized).^[3]

Causes

Cancers are primarily an environmental disease with 90–95% of cases attributed to environmental factors and 5–10% due to genetics. Common environmental factors that contribute to cancer death include tobacco (25–30%), diet and obesity (30–35%), infections (15–20%), radiation (both ionizing and non-ionizing, up to 10%), stress, lack of physical activity, and environmental pollutants.^[4]

1. Chemicals

The incidence of lung cancer is highly correlated with smoking. Cancer pathogenesis is traceable back to DNA mutations that impact cell growth and metastasis. Substances that cause DNA mutations are known as mutagens, and mutagens that cause cancers are known as Carcinogens. Particular substances have been linked to specific types of cancer. Tobacco smoking is associated with many forms of cancer, and causes 90% of lung cancer.

Many mutagens are also carcinogens, but some carcinogens are not mutagens. Alcohol is an example of a chemical carcinogen that is not a mutagen. Tobacco is responsible for about one in three of all cancer deaths in the developed world, and about one in five worldwide.^[5]

2. Diet and exercise

Diet, physical inactivity, and obesity are related to approximately 30–35% of cancer deaths. Physical inactivity is believed to contribute to cancer risk not only through its effect on body weight but also through negative effects on immune system and endocrine system. More than half of the effect from diet is due to over nutrition rather than from eating too little healthy foods. For example, gastric cancer is more common in Japan due to its high-salt diet and colon cancer is more common in the United States.^[6]

3. Infection

Worldwide approximately 18% of cancer deaths are related to infectious diseases. Viruses are the usual infectious agents that cause cancer but bacteria and parasites may also have an effect. A virus that can cause cancer is called an oncovirus. These include human papillomavirus (cervical carcinoma), Epstein–Barr virus (B-cell lymphoproliferative disease and nasopharyngeal carcinoma), Kaposi's sarcoma herpes virus (Kaposi's sarcoma and primary effusion lymphomas), hepatitis B and hepatitis C viruses (hepatocellular carcinoma), and Human T-cell leukemia virus-1 (T-cell leukemias). Bacterial infection may also increase the risk of cancer, as seen in *Helicobacter pylori*-induced gastric carcinoma. Parasitic infections strongly associated with cancer include *Schistosoma haematobium* (squamous cell carcinoma of the bladder) and the liver flukes, *Opisthorchis viverrini* and *Clonorchis sinensis* (cholangiocarcinoma).^[7]

4. Radiation

Up to 10% of invasive cancers are related to radiation exposure, including both ionizing radiation and non-ionizing ultraviolet radiation. Sources of ionizing radiation include medical

imaging, and radon gas. Radiation can cause cancer in most parts of the body, in all animals, and at any age, although radiation-induced solid tumors usually take 10–15 years, and can take up to 40 years, to become clinically manifest, and radiation-induced leukemias typically require 2–10 years to appear. Some people, such as those with nevoid basal cell carcinoma syndrome or retinoblastoma, are more susceptible than average to developing cancer from radiation exposure. Children and adolescents are twice as likely to develop radiation-induced leukemia as adults; radiation exposure before birth has ten times the effect. Ionizing radiation is not a particularly strong mutagen. Residential exposure to radon gas, for example, has similar cancer risks as passive smoking. Low-dose exposures, such as living near a nuclear power plant, are generally believed to have no or very little effect on cancer development⁷.

5. Heredity

Hereditary cancers are primarily caused by an inherited genetic defect. Less than 0.3% of the population are carriers of a genetic mutation which has a large effect on cancer risk and these causes less than 3–10% of all cancer. Some of these syndromes include: certain inherited mutations in the genes BRCA1 and BRCA2 with a more than 75% risk of breast cancer and ovarian cancer, and hereditary nonpolyposis colorectal cancer (HNPCC or Lynch syndrome) which is present in about 3% of people with colorectal cancer, among others⁷.

6. Physical agents

Some substances cause cancer primarily through their physical, rather than chemical, effects on cells. A prominent example of this is prolonged exposure to asbestos, naturally occurring mineral fibers which are a major cause of mesothelioma, which is a cancer of the serous membrane, usually the serous membrane surrounding the lungs. Other substances in this category, including both naturally occurring and synthetic asbestos-like fibers such as wollastonite, attapulgite, glass wool, and rock wool, are believed to have similar effects. Non-fibrous particulate materials that cause cancer include powdered metallic cobalt and nickel, and crystalline silica (quartz, cristobalite, and tridymite).^[7]

7. Hormones

Some hormones play a role in the development of cancer by promoting cell proliferation. Insulin-like growth factors and their binding proteins play a key role in cancer cell proliferation, differentiation and apoptosis, suggesting possible involvement in carcinogenesis. Hormones are important agents in sex-related cancers such as cancer of the breast, endometrium, prostate, ovary, and testis, and also of thyroid cancer and bone cancer.^[8]

Pathophysiology

Cancers are caused by a series of mutations. Each mutation alters the behavior of the cell somewhat.

1. Genetic Alterations

Cancer is fundamentally a disease of tissue growth regulation failure. In order for a normal cell to transform into a cancer cell, the genes which regulate cell growth and differentiation must be altered. The affected genes are divided into two broad categories. Oncogenes are genes which promote cell growth and reproduction. Tumor suppressor genes are genes which inhibit cell division and survival. Malignant transformation can occur through the formation of novel oncogenes, the inappropriate over-expression of normal oncogenes, or by the under-expression or disabling of tumor suppressor genes. Typically, changes in many genes are required to transform a normal cell into a cancer cell. Genetic changes can occur at different levels and by different mechanisms. The gain or loss of an entire chromosome can occur through errors in mitosis. More common are mutations, which are changes in the nucleotide sequence of genomic DNA.^[9]

Large-scale mutations involve the deletion or gain of a portion of a chromosome. Genomic amplification occurs when a cell gains many copies (often 20 or more) of a small chromosomal locus, usually containing one or more oncogenes and adjacent genetic material. Translocation occurs when two separate chromosomal regions become abnormally fused, often at a characteristic location.

Small-scale mutations include point mutations, deletions, and insertions, which may occur in the promoter region of a gene and affect its expression, or may occur in the gene's coding sequence and alter the function or stability of its protein product. Disruption of a single gene may also result from integration of genomic material from a DNA virus or retrovirus, and resulting in the expression of viral oncogenes in the affected cell and its descendants. Replication of the enormous amount of data contained within the DNA of living cells will probabilistically result in some errors (mutations).^[10,11]

2. Epigenetic Alterations

Epigenetic alterations refer to functionally relevant modifications to the genome that do not involve a change in the nucleotide sequence. Examples of such modifications are changes in DNA methylation (hypermethylation and hypomethylation) and histone modification and

changes in chromosomal architecture (caused by inappropriate expression of proteins such as HMGA2 or HMGA1). Each of these epigenetic alterations serves to regulate gene expression without altering the underlying DNA sequence. These changes may remain through cell divisions, last for multiple generations, and can be considered to be epimutations (equivalent to mutations). Epigenetic alterations occur frequently in cancers. As an example, Schneckenger and Diederich listed protein coding genes that were frequently altered in their methylation in association with colon cancer. While large numbers of epigenetic alterations are found in cancers, the epigenetic alterations in DNA repair genes, causing reduced expression of DNA repair proteins, may be of particular importance. Such alterations are thought to occur early in progression to cancer and to be a likely cause of the genetic instability characteristic of cancers.^[12-13]



Diagnosis

Most cancers are initially recognized either because of the appearance of signs or symptoms or through screening. Neither of these lead to a definitive diagnosis, which requires the examination of a tissue sample by a pathologist. People with suspected cancer are investigated with medical tests. These commonly include blood tests, X-rays, CT scans and endoscopy. Most people are distressed to learn that they have cancer. They may become extremely anxious and depressed. The risk of suicide in people with cancer is approximately double the normal risk.^[14-16]

Classification

Cancers are classified by the type of cell that the tumor cells resemble and is therefore presumed to be the origin of the tumor. These types include.

- **Carcinoma**

Cancers derived from epithelial cells. This group includes many of the most common cancers, particularly in the aged, and include nearly all those developing in the breast, prostate, lung, pancreas, and colon.

- **Sarcoma**

Cancers arising from connective tissue (i.e. bone, cartilage, fat, nerve), each of which develop from cells originating in mesenchymal cells outside the bone marrow.

- **Lymphoma and leukemia**

These two classes of cancer arise from hematopoietic (blood-forming) cells that leave the marrow and tend to mature in the lymph nodes and blood, respectively. Leukemia is the most common type of cancer in children accounting for about 30%.

- **Germ cell tumor**

Cancers derived from pluripotent cells, most often presenting in the testicle or the ovary (seminoma and dysgerminoma, respectively).

- **Blastoma**

Cancers derived from immature "precursor" cells or embryonic tissue. Blastomas are more common in children than in older adults.^[17-18]

Principles of Chemotherapy

Many forms of chemotherapy are targeted at the process of cell division. The rationale being that cancer cells are more likely to be replicating than normal cells. Unfortunately as their action is not specific, they are associated with significant toxicity. An understanding of the principles of tumour biology and cellular kinetics is helpful to appreciate the mechanisms of action of cancer chemotherapy.

1. Classification of Chemotherapeutic Agents

1. Phase-Specific Chemotherapy

These drugs, such as methotrexate and vinca alkaloids, kill proliferating cells only during a specific part or parts of the cell cycle. Antimetabolites, such as methotrexate, are more active against S-phase cells (inhibiting DNA synthesis) whereas vinca alkaloids are more M-phase specific (inhibiting spindle formation and alignment of chromosomes). Vinblastine can arrest cells in mitosis. These synchronized cells enter the S-phase together and can be killed by a phase-specific agent, such as cytosine arabinoside.^[19, 20]

2. Cell Cycle-Specific Chemotherapy

Most chemotherapy agents are cell cycle-specific, meaning that they act predominantly on cells that are actively dividing. They have a dose-related plateau in their cell killing ability because only a subset of proliferating cells remain fully sensitive to drug-induced cytotoxicity at any one time. The way to increase cell kill is therefore to increase the duration of exposure rather than increasing the drug dose.^[19-20]

3. Cell Cycle-Nonspecific Chemotherapy

These drugs, for example alkylating agents and platinum derivatives, have an equal effect on tumour and normal cells whether they are in the proliferating or resting phase. They have a linear dose–response curve; that is, the greater the dose of the drug, the greater the fractional cell kill.^[19-20]

2. Limitations of Cytotoxic Agents

There are a number of problems with the safety profile and efficacy of chemotherapeutic agents. Cytotoxics predominantly affect rapidly dividing cells so do not specifically target cancer cells in the resting phase. They also only influence a cell's ability to divide and have little effect on other aspects of tumour progression such as tissue invasion, metastases or progressive loss of differentiation. Finally, cytotoxics are associated with a high incidence of adverse effects. The most notable examples include bone marrow suppression, alopecia, mucositis, nausea and vomiting.^[18-19]

3. Other Novel Treatments

There are now a large number of new types of agents entering all phases of clinical trials. To date, they have met with variable success. It is important to mention a few drugs which have really made an impact on treatment of specific cancers in the last few years.

- Trastuzumab (Herceptin): A humanized monoclonal antibody against the HER-2 receptor which is now becoming increasingly important in the treatment of both locally advanced and metastatic breast cancer.
- Ritiximab (Mabthera): The rituximab antibody is a genetically engineered chimeric murine/human monoclonal antibody directed against the CD20 antigen found on the surface of normal and malignant B lymphocytes. It is being increasingly used in combination with chemotherapy to manage many different types of indolent and aggressive B-cell lymphomas.^[17-19]

Nanotechnological Approach towards Cancer

Nanotechnology refers to the interactions of cellular and molecular components and engineered materials - typically clusters of atoms, molecules, and molecular fragments - at the most elemental level of biology. Such nanoscale objects - typically, though not exclusively, with dimensions smaller than 100 nanometers - can be useful by themselves or as part of larger devices containing multiple nanoscale objects. At the nanoscale, the physical, chemical, and biological properties of materials differ fundamentally and often unexpectedly from those of the corresponding bulk material because the quantum mechanical properties of atomic interactions are influenced by material variations on the nanometer scale. In fact, by creating nanometer-scale structures, it is possible to control fundamental characteristics of a material, including its melting point, magnetic properties, and even color, without changing the material's chemical composition.^[20-22]

The six major challenge areas of emphasis include**1. Prevention and Control of Cancer**

- Developing nanoscale devices that can deliver cancer prevention agents.
- Designing multicomponent anticancer vaccines using nanoscale delivery vehicles.

2. Early Detection and Proteomics

- Creating implantable, biofouling-indifferent molecular sensors that can detect cancer-associated biomarkers that can be collected for ex vivo analysis or analyzed in situ, with the results being transmitted via wireless technology to the physician.
- Developing “smart” collection platforms for simultaneous mass spectroscopic analysis of multiple cancer-associated markers.

3. Imaging Diagnostics

- Designing “smart” injectable, targeted contrast agents that improve the resolution of cancer to the single cell level.
- Engineering nanoscale devices capable of addressing the biological and evolutionary diversity of the multiple cancer cells that make up a tumor within an individual.

4. Multifunctional Therapeutics

- Developing nanoscale devices that integrate diagnostic and therapeutic functions.
- Creating “smart” therapeutic devices that can control the spatial and temporal release of therapeutic agents while monitoring the effectiveness of these agents.

5. Quality of Life Enhancement in Cancer Care

- Designing nanoscale devices that can optimally deliver medications for treating conditions that may arise over time with chronic anticancer therapy, including pain, nausea, loss of appetite, depression, and difficulty breathing.

6. Interdisciplinary Training

- Coordinating efforts to provide cross-training in molecular and systems biology to nanotechnology engineers and in nanotechnology to cancer researchers.
- Creating new interdisciplinary coursework/degree programs to train a new generation of researchers skilled in both cancer biology and nanotechnology.^[23-27]

Nanotechnology and Diagnostics

Today, cancer-related nanotechnology research is proceeding on two main fronts:

- Laboratory-based diagnostics and
- In vivo diagnostics and therapeutics.

Following are the new and upcoming concepts for Diagnosis of Cancer and detection of tumour in body.

1. Clinically-translated silica nanoparticles as dual-modality cancer-targeted probes for image-guided surgery and interventions

Clinically-translated ^{124}I -cRGDY-PEG-C dots, coupled with PET and portable optical camera devices, can overcome limitations associated with current SLN mapping procedures.

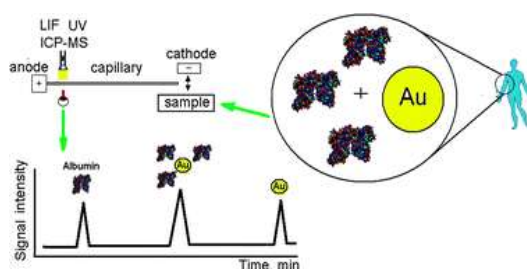


Early diagnosis and treatment of melanoma are essential to minimizing morbidity and mortality. The presence of lymph node metastases is a vital prognostic predictor, and accurate identification by imaging has important implications for disease staging, prognosis, and

clinical outcome. Sentinel lymph node (SLN) mapping procedures are limited by a lack of Intraoperative visualization tools that can aid accurate determination of disease spread and delineates nodes from adjacent critical neural and vascular structures.^[28]

2. Interactions of tumour-targeting nanoparticles with proteins: potential of using capillary electrophoresis as a direct probe

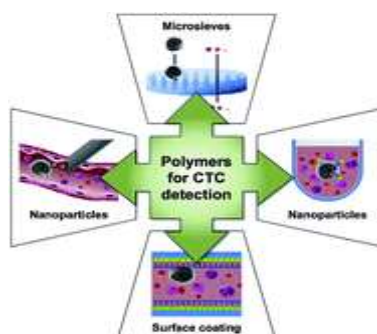
The potential of capillary electrophoresis in studying reactions associated with protein-mediated transformations of metal-based nanoparticles is highlighted. Metal-based nanoscale particles possess unique optoelectronic or magnetic properties that make them highly promising as imaging agents in cancer therapy research. The fate of nanoparticles in vivo and particularly, the delivery to tumours are closely related to their interactions with plasma proteins. Furthermore, proteins can be used to modify the nanoparticle surface in order to facilitate active targeting to tumours.^[29]



3. The role of polymers in detection and isolation of circulating tumor cells

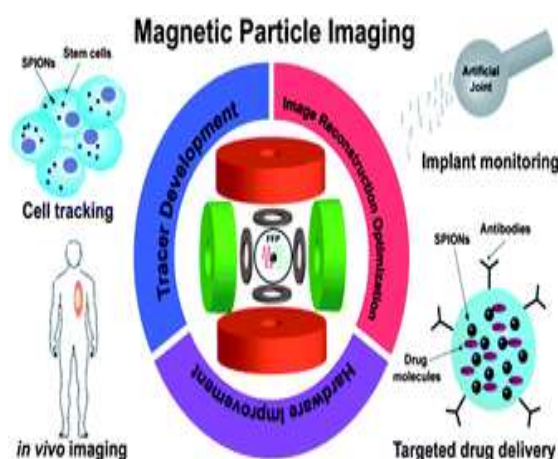
Circulating tumor cells (CTCs) in blood, known to be responsible for cancer metastasis, have been widely investigated as a biomarker for diagnosis and prognosis of metastatic cancer.

Circulating tumor cells (CTCs) in blood, known to be responsible for cancer metastasis, have been widely investigated as a biomarker for diagnosis and prognosis of metastatic cancer. In many of the studies, polymers have been commonly used to enable or enhance separation of CTCs; however, existing reviews do not focus on the role that has been played by polymers in the CTC detection field.^[30]



4. Magnetic particle imaging: advancements and perspectives for real-time in Vivo monitoring and image-guided therapy

Magnetic particle imaging (MPI) is an emerging biomedical imaging technology that allows the direct quantitative mapping of the spatial distribution of super paramagnetic iron oxide nanoparticles. MPI's increased sensitivity and short image acquisition times foster the creation of tomographic images with high temporal and spatial resolution. The contrast and sensitivity of MPI is envisioned to transcend those of other medical imaging modalities presently used, such as magnetic resonance imaging (MRI), X-ray scans, ultra sound, computed tomography (CT), positron emission tomography (PET) and single photon emission computed tomography (SPECT).^[31]



5. Glyconanotechnology

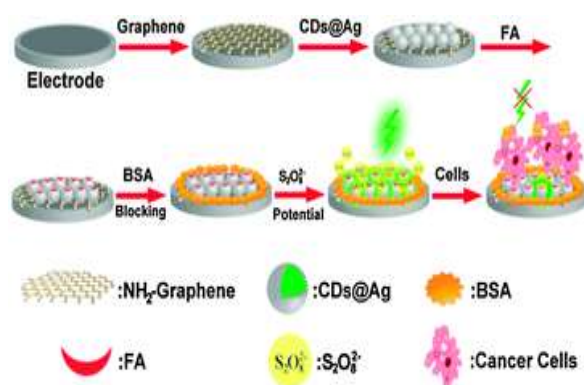
The most recent developments of glyconano materials for drug design, vaccine development, molecular imaging, enzyme inhibition and biosensors are critically discussed.

Glyconanotechnology can be seen as the synergy between nanotechnology and glycan related biological and medical problems.^[32]



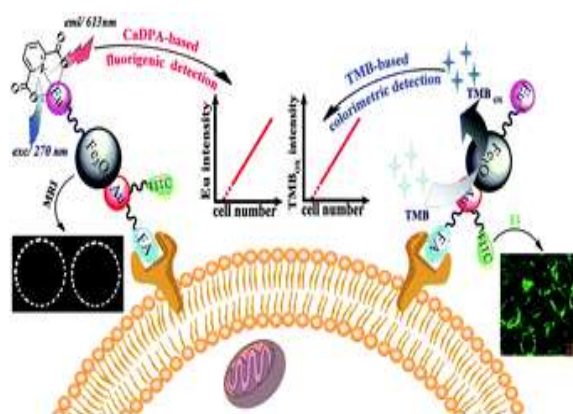
6. Highly sensitive electrochemiluminescent cytosensing using carbon nanodot@Ag hybrid material and graphene for dual signal amplification

Functionalized carbon nanodots (C-dots) were used as novel electrochemiluminescence (ECL) probes for highly sensitive and selective detection of cancer cells. Here we use functionalized carbon nanodots (C-dots) as novel electrochemiluminescence (ECL) probes and graphene nanosheets as signal amplification agents for highly sensitive and selective cancer cell detection. The ECL cytosensor shows superior cell-capture ability and exhibits a wide linear range and a low detection limit for cancer cells.^[33]



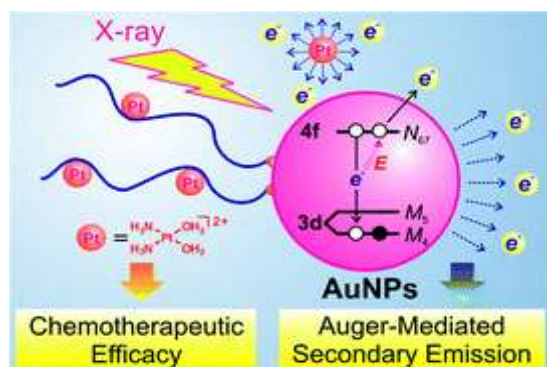
7. A multifunctional nanoprobe based on Au-Fe₃O₄ nanoparticles for multimodal and ultrasensitive detection of cancer cells

A multifunctional nanoprobe, which can be used for dual modal imaging and the detection of cancer cells, has been reported.^[34]



8. Surface-engineered nanomaterials as X-ray absorbing adjuvant agents for Auger-mediated chemo-radiation

Pt^{II}-tethered gold nanoparticles demonstrate therapeutic potential as an adjuvant agent for chemo-radiation, exhibiting both chemotherapeutic potency and Auger-electron emission.^[35]



9. Micellar nanoparticle formation via electrostatic interactions for delivering multinuclear platinum(II) drugs

Nanoparticles formed via electrostatic interactions between methoxy-polyethylene glycol-block-poly(glutamic acid) (MPEG-PGA) and a multinuclear platinum(II) drug, di-cisPt.

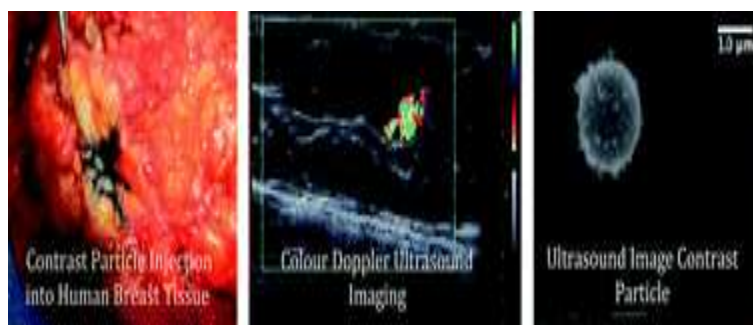


10. Exploring the fluorescence switching phenomenon of curcumin encapsulated niosomes: in vitro real time monitoring of curcumin release to cancer cells

This is the first report on the real time monitoring of the release of curcumin to a cancer cell line through a fluorescence switching phenomenon of curcumin encapsulated niosomes, which exhibited strong blue and green color fluorescence in the UV and visible regions respectively. This is the first report on the reversible fluorescence switching of curcumin encapsulated niosomes exhibiting a strong blue color excimer emission in the UV region and a green color luminescence of the excited state monomer form of curcumin that undergoes ESIPT in the visible region. The real time monitoring of the release of curcumin from niosomes is feasible through the change of fluorescence color from blue to green.^[36]

11. Hard shell gas-filled contrast enhancement particles for colour Doppler ultrasound imaging of tumors

Perfluorocarbon vapour-filled boron-doped hollow silica microshells and nanoshells provide a new rigid inorganic platform for ultrasound image contrast enhancement.^[37]

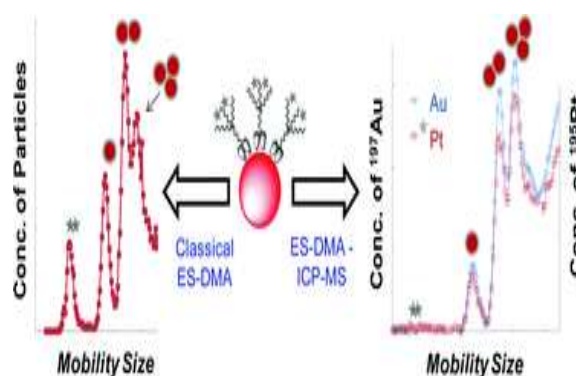


Hollow hard shell particles of 200 nm and 2 micron diameter with a 10 nm thick porous silicashell have been synthesized using polystyrene templates and a sol–gel process. The template ensures that the hollow particles are monodispersed, while the charged silica surface ensures that they remain suspended in solution for weeks. When filled with perfluorocarbon gas, the particles behave as an efficient contrast agent for colour Doppler ultrasound imaging in human breast tissue. The silica shell provides unique properties compared to conventional soft shell particles employed as ultrasound contrast agents: uniform size control, strong adsorption to tissue and cells immobilizing particles at the tissue injection site, a long imaging lifetime, and a silica surface that can be easily modified with biotargeting ligands or small molecules to adjust the surface charge and polarity.^[37]

12. Quantitative analysis of dendron-conjugated cisplatin-complexed gold nanoparticles using scanning particle mobility mass spectrometry

In situ size-resolved analysis of anti-tumor drug loading on a model nanoparticle-based therapeutic, with detection and quantification of aggregate states.

Study demonstrates a prototype methodology to provide traceable quantification and to determine other important formulation factors relevant to therapeutic performance.^[38]

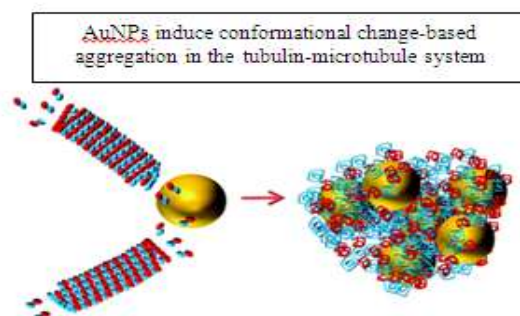


13. Facile preparation of multifunctional hollow silica nanoparticles and their cancer specific targeting effect

A unique and simple method was established for fabrication of multifunctional silica nanoparticles with superior cancer-specific targeting and imaging properties. Efficient delivery of therapeutics to tumor cells is one of the key issues in cancer therapy.^[39]

14. Unprecedented inhibition of tubulin polymerization directed by gold nanoparticle inducing cell cycle arrest and apoptosis

The effect of gold nanoparticles (AuNPs) on the polymerization of tubulin has not been examined till now. We report that interaction of weakly protected AuNPs with microtubules (MTs) could cause inhibition of polymerization and aggregation in the cell free system. We estimate that single citrate capped AuNPs could cause aggregation of $\sim 10^5$ tubulin hetero dimers. Investigation of the nature of inhibition of polymerization and aggregation by Raman and Fourier transform-infrared (FTIR) spectroscopies indicated partial conformational changes of tubulin and microtubules, thus revealing that AuNP-induced conformational change is the driving force behind the observed phenomenon. Study also concomitant apoptosis. These would be useful in the understanding of cancer therapeutics and safety of nanomaterials.^[40]



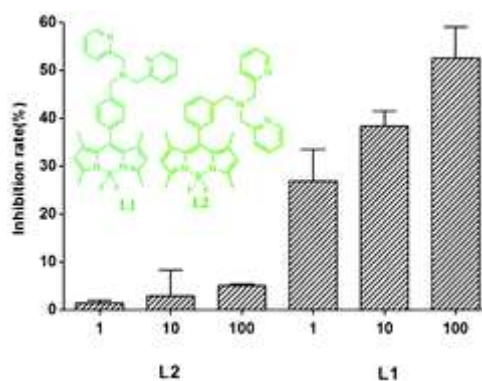
15. A facile synthesis of strong near infrared fluorescent layered double hydroxide nanovehicles with an anticancer drug for tumor optical imaging and therapy

A facile method to fabricate a multi-functional bio-LDH system for simultaneous tumor optical imaging and therapy is developed. A new multifunctional nanovehicle for tumor optical imaging and therapy was developed using $\text{Y}_2\text{O}_3:\text{Er}^{3+}$, Yb^{3+} nanoparticles as near infrared fluorescent nanophosphors, and MgAl-layered double hydroxide (LDH) nanosheets as anticancer drug nanovehicles. Mono-dispersed $\text{Y}_2\text{O}_3:\text{Er}^{3+}$,

Yb^{3+} nanophosphors were readily synthesized by the urea assisted homogenous precipitation method. A better anticancer efficiency was obtained over the nanovehicles than the free drug which can be attributed to their positively charged surfaces for favorable interaction with the negatively charged cell membranes. The multifunctional nanovehicles designed in this work are expected to be promising material candidates for simultaneous tumor optical imaging and therapy.^[41]

16. Multifunctional BODIPY derivatives to image cancer cells and sense copper (II) ions in living cells

Two multifunctional colorimetric and fluorescent chemosensors were synthesized by the conjugation of BODIPY (4,4-difluoro-1, 3, 5, 7-tetramethyl-4-bora-3a, 4a-diaza-s-indacene) and di (2-picolyl) amine with benzyl groups (para-substituted, **L1**; meta-substituted, **L2**) as spacers, for selectively sensing copper(II) ions in preference to a variety of other common metal ions in aqueous media. The two analogous compounds exhibit different cytotoxic behaviour and attenuate mitochondrial membrane potentials in HepG-2 cells. In vitro bioassay results demonstrate that only **L2** causes the decrease of mitochondrial membrane potentials in HepG-2 cells with low toxicity. Furthermore, fluorescence imaging in vitro confirms that **L2** is a low toxicity chemosensor for copper(II) ions in living cells.^[42]



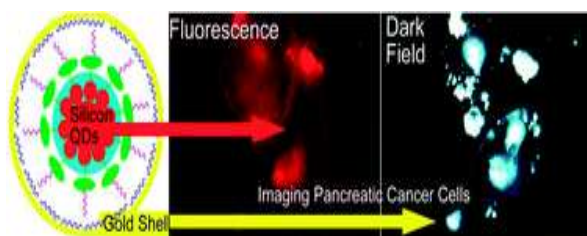
17. Highly luminescent water-soluble quaternary Zn–Ag–In–S quantum dots for tumor cell-targeted imaging

Here a facile approach to produce water-soluble (cadmium-free) quaternary Zn–Ag–In–S (ZAIS) QDs. Their efficient photoluminescence (PL) emissions can be tuned widely in the range of 525–625 nm by controlling the size and composition of the QDs with the PL quantum yields (QYs) of 15–30%. These highly luminescent ZAIS QDs are less toxic due to

the absence of highly toxic cadmium, and can be versatily modified by a DHLA-PEG-based ligand. Importantly, after being modified by tumor cell-specific targeting ligands (e.g., folate and RGD peptide), the PEGylated quaternary QDs show potential applications in tumor cell imaging as a promising alternative for Cd-based QDs.^[43]

18. Evaluation of the shear force of single cancer cells by vertically aligned carbon nanotubes suitable for metastasis diagnosis

carbon nanotube arrays have been demonstrated as probes for rapid quantifying of cancer cell deformability for metastasis diagnosis. vertically aligned carbon nanotube (VACNT) arrays have been demonstrated as probes for rapid quantifying of cancer cell deformability with high resolution. Nanotube-based methodology for quantifying the single cell mechanical behavior, which could be useful for understanding the metastatic behavior of cells.^[44]



19. Quantification of ovarian cancer markers with integrated microfluidic concentration gradient and imaging nanohole surface plasmon resonance

Nanohole arrays are integrated into a microfluidic gradient generator for detection of ovarian cancer biomarkers via SPR imaging. Nanohole array-based biosensors integrated with a microfluidic concentration gradient generator were used for imaging detection and quantification of ovarian cancer markers.^[45]

20. Detection of cancer cells using a peptide nanotube-folic a peptide nanotube-folic acid modified grapheme electrode

This describes the preparation of a graphene electrode modified with a new conjugate of peptide nanotubes and folic acid for the selective detection of human cervical cancer cells over-expressing folate receptors. The modified electrode opens up new possibilities for future applications in early stage diagnoses of diseases where cells over-express folate receptors, such as in cancer or leishmaniasis disease.^[46]

21. Plasmonic gold and luminescent silicon nano platforms for multimode imaging of cancer cells


A schematic of a nanoprobe composed of silicon quantum dots in the core of a F127 pluronic micelle coated with a gold shell. The nanoprobe is used for fluorescent and dark-field imaging of pancreatic cancer cells. The fluorescent and dark field micrographs indicate that the probe can be used for multimode imaging. The development of multimodal nanoparticle platforms is desirable for cancer nanotechnology applications. Creating single nanoplateforms with both plasmonic and photoluminescent optical properties has remained a challenge, because combining discrete entities each having one of these unique properties typically results in the attenuation of one of the desirable properties. The result is a nano platform with both plasmonic and luminescent properties in a useful form.^[47]

22. Sensitive sandwich ELISA based on a gold nanoparticle layer for cancer detection

This simple and cost-effective gold nanoparticle layer (GNPL)-based sandwich ELISA holds promise in clinical applications. The availability of techniques for the sensitive detection of early stage cancer is crucial for patient survival. In this, a GNPL-based sandwich format ELISA was developed, which showed superiority in terms of detection limit and sensitivity in the determination of rabbit IgG in buffer. More importantly, experiments using plasma spiked with carcino embryonic antigen (CEA) as a representative biomarker showed that our GNPL-based ELISA assay amplified the signal and lowered the LOD compared to other assays, including commercialized CEA ELISA kits. This simple and cost-effective GNPL-based sandwich ELISA holds promise in clinical applications.^[48]

Nanotechnology and Cancer Therapy

Nanoscale devices have the potential to radically change cancer therapy for the better and to dramatically increase the number of highly effective therapeutic agents.

 Following are the new concepts of nanotechnology for cancer therapy.

1. Targeting carbon nanotubes against cancer

Carbon nanotubes offer new opportunities in the struggle against cancer.

The use of carbon nanotubes (CNTs) as polyvalent tools for cancer treatment is progressing at a very fast pace. The most promising approach is the targeted delivery of drugs, designed to selectively direct the therapeutic treatment towards the tumours. CNTs may offer several

advantages to overcome one of the main limitations of most existing anticancer therapies, namely the lack of selectivity.^[49]

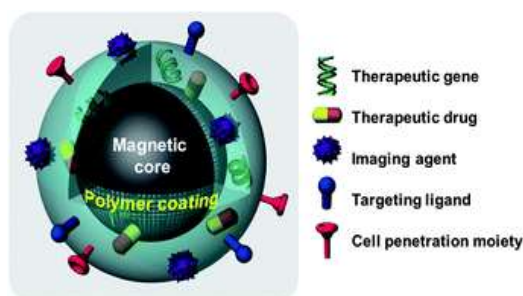


2. Bionanomaterials for bone tumor engineering and tumor destruction

Bionanomaterial-based bone cancer treatment offers hope for treating bone cancer and provides many exciting possibilities to enable important new therapeutic outcomes. Physicists, chemists, engineers, biologists, and clinicians will continue to address research questions at the level of fundamental biology and science to develop novel biomaterials and systems, particularly enabling cost-effective and large-scale production of multifunctional nanomaterial systems. A new class of anticancer compounds, e.g., geminal bisphosphonates, that has been shown to have strong affinity towards various hydroxyapatite-based bone scaffolds with controlled adsorption and release for anticancer activity.^[50]

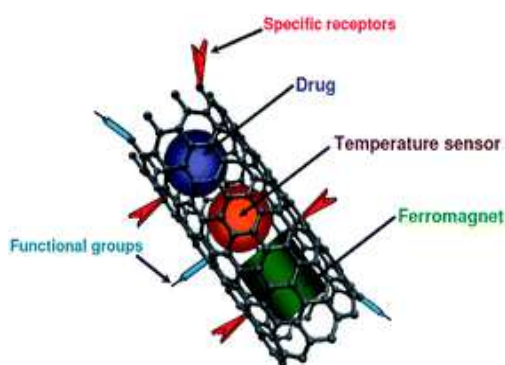
3. Magnetic nanocomplexes and the physiological challenges associated with their use for cancer imaging and therapy

Magnetic nanoparticles offer potential advances in cancer treatment. One example is cancer theranostics, which refers to the combination of a diagnostic tool, i.e., magnetic resonance (MR) imaging, and therapeutic entities such as drugs, oligonucleotides, antibodies, and peptides. They can be conjugated with bioactive molecules and have the ability to form amagnetic field gradient under an external magnetic field. They can offer a variety of active drug delivery and imaging strategies along with modalities such as magnetic hyperthermia. Imaging with magnetic nanoparticles can facilitate more effective cancer therapy through more well informed decision-making. Discuss about the bioapplications of magnetic nanoparticles in simultaneous cancer imaging and therapy.^[51]



4. Carbon nanostructures as multi-functional drug delivery platforms

Examines the properties of carbon nanostructures that make them attractive structures for a new generation of multi-drug delivery platforms. Nanotechnology is providing exciting and new opportunities which are likely to revolutionize future clinical practice. The use of nanoparticles for biomedical applications is particularly exciting due to their huge potential for multi-modal approaches. This includes their use as drug delivery vectors, imaging contrast agents, hyperthermia systems and molecular targeting. Their ability to cross biological barriers, for example the blood brain barrier, makes them attractive for potential treatments in neurological disorders. There is also great hope that nanostructures will serve as platforms in future cancer therapies. Current cancer fighting strategies consist primarily of surgery, radiation therapy and chemotherapy. Each of these treatments is bound by a limit, known as the therapeutic window, which, if exceeded, causes undue harm to the patient. In this context, carbon nanostructures are amongst the leading contenders as building blocks to deliver multi-function drug delivery platforms.^[52]

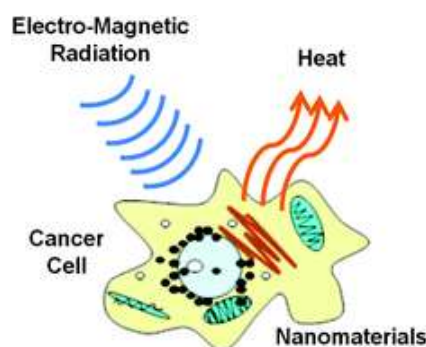


5. Progress in materials for thermal ablation of cancer cells

Nanomaterials have excellent abilities to act as thermal agents under electromagnetic-radiation excitation, representing the foundation for complex clinical disease treatments.

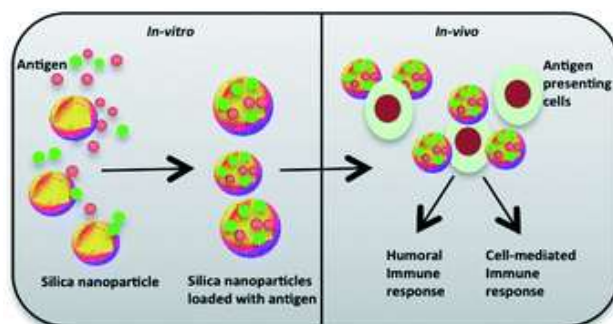
Owing to the complexity of cancer biology, successful treatments must make use of multidisciplinary approaches that include genetic biology, materials science, chemistry, and physics. The development of nanotechnology as a mature science has provided new tools for the early detection and treatment of cancer by combining the synthesis of multifunctional nanosystems with the advanced capability of the targeted delivery of drugs and genes down to a single cell level. Nanomaterials with their unique optical, magnetic, and electrical properties have proven to be excellent candidates as thermal agents under the excitation of various electromagnetic fields (laser, alternating magnetic fields, or radiofrequency) that are

capable of producing enough thermal energy for the specific destruction of the cancer cells both in vitro and in vivo. As a result, the use of such nanomaterials could open a new field in the area of cancer medicine given their ability to act as high resolution contrast agents and to thermally ablate tumors or individual cancer cells and to overcome some of the current limitations in cancer treatment.^[53]



6. Mesoporous silica nanoparticles as antigen carriers and adjuvants for vaccine delivery

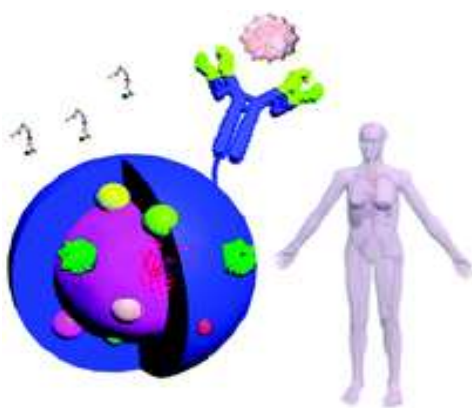
Vaccines have been at the forefront of improving human health for over two centuries. The challenges faced in developing effective vaccines flow from complexities associated with the immune system and requirement of an efficient and safe adjuvant to induce a strong adaptive immune response. Development of an efficient vaccine formulation requires careful selection of a potent antigen, efficient adjuvant and route of delivery. Adjuvants are immunological agents that activate the antigen presenting cells (APCs) and elicit a strong immune response. In the past decade, the use of mesoporous silica nanoparticles (MSNs) has gained significant attention as potential delivery vehicles for various biomolecules.^[54]



7. Cytokines as biomarkers of nanoparticle immunotoxicity

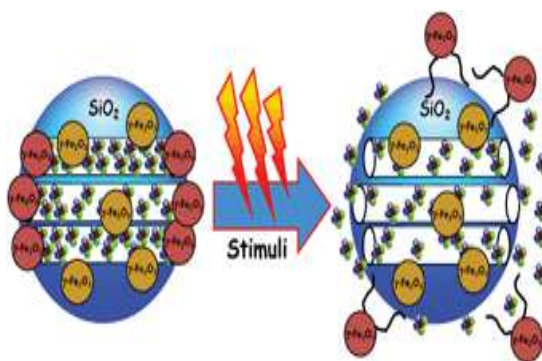
Cytokines induced upon in vitro and in vivo administration of nanomaterials can be utilized as biomarkers of nanoparticle immunotoxicity.

Cytokines perform pleiotropic functions to mediate and regulate the immune response and are generally recognized as biomarkers of immunotoxicity. While the specificity and validity of certain cytokines as markers of adverse immune response has been established for chemicals, small and macro-molecular drugs, research on their applicability for predicting and monitoring the immunotoxicity of engineered nanomaterials is still ongoing. The goal of this review is to provide guidelines as to important cytokines that can be utilized for evaluating the immunotoxicity of nanomaterials and to highlight the role of those cytokines in mediating adverse reactions, which is of particular importance for the clinical development of nanopharmaceuticals and other nanotechnology-based products.^[55]



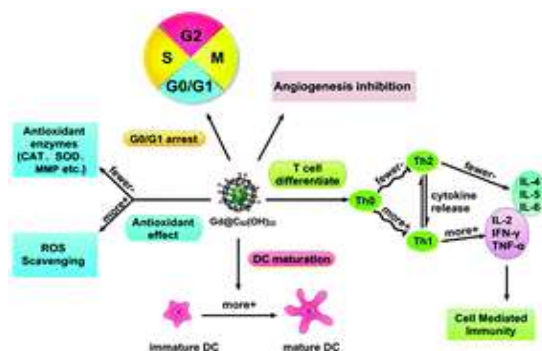
8. Mesoporous silica nanoparticles for the design of smart delivery nanodevices

Mesoporous silica nanoparticles (MSNPs) are receiving growing attention by the scientific community for their ground breaking potential in nanomedicine. This review describes research efforts to combine MSNPs, stimuli-responsive nanocaps and magnetic nanoparticles aimed at designing innovative nanodevices whose characteristics and performance can be tuned attending to specific clinical needs.^[56]



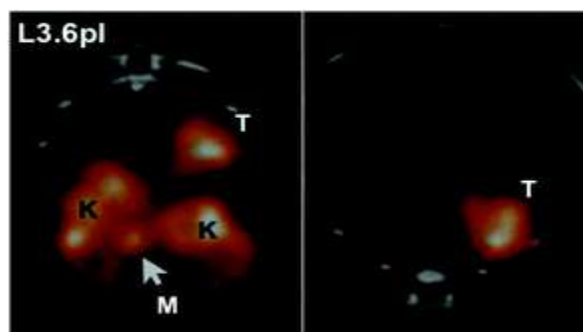
9. Biological characterizations of nanoparticles as fullerene derivatives for cancer therapy

Biological characterizations and mechanisms analysis of $[\text{Gd}@\text{C}_{82}(\text{OH})_{22}]_n$ nanoparticles as fullerene derivatives for cancer therapy.^[57]



10. Targeted nanoparticles in imaging: paving the way for personalized medicine in the battle against cancer

It shows unique characteristics of cancer that allow for nanoparticle imaging in vivo.^[58]



11. Towards biocompatible nanovalves based on mesoporous silica nanoparticles

Biocompatible nanovalves effectively store/protect drugs inside nano-reservoirs, then deliver and release them to kill targeted cancer cells under external stimuli. Nanoparticles show great potential as superior intelligent drug delivery platforms. Among them, mesoporous silica nanoparticles (MSNs) are particularly interesting candidates for powerful drug carriers because of their unique characteristics and abilities to efficiently and specifically entrap cargo molecules. Recent research progress on MSN-based smart materials that can simultaneously address targeted delivery of anticancer drugs, ideally “zero premature release”, and controlled release by external physical, chemical and biological stimuli.^[59]

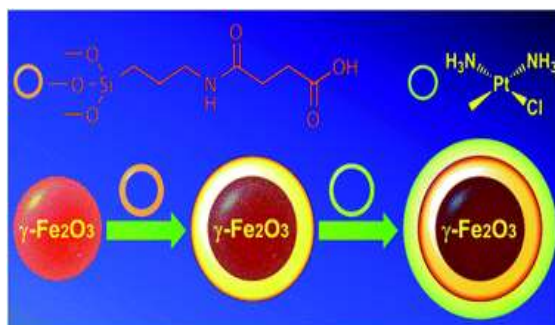


12. Lipid-coated nanoscale coordination polymers for targeted delivery of antifolates to cancer cells

Nanoscale coordination polymers (NCPs) have been demonstrated as an interesting platform for drug delivery, as they possess many advantages over small-molecule chemo-therapeutics such as high payloads, lower systemic toxicity, tunability, and enhanced tumor uptake. Existing formulations for the delivery of methotrexate (MTX), an antifolate cancer drug, have very low drug loadings. Herein, we report the incorporation of MTX as a building block in an NCP formulation with exceptionally high drug loadings (up to 79.1 wt %) and the selective delivery of the NCP to cancer cells. Encapsulation of the NCP in a functionalized lipid bilayer allows for targeted delivery and controlled release to cancer cells. A phosphor can be doped into the NCPs for monitoring particle uptake by optical imaging. The lipid-coated and anisamide-targeted NCPs have superior in vitro efficacy against acute lymphoblastic leukemia cells when compared to the free drug.^[60]

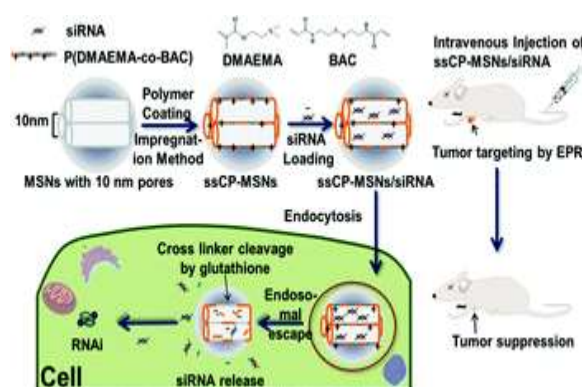
13. A platinum anticancer theranostic agent with magnetic targeting potential derived from maghemite nanoparticles

A cisplatin-tethered superparamagnetic nanocomposite with antitumor and magnetic resonance imaging properties preferentially accumulates in tumor tissues in the presence of an external magnetic field. Super paramagnetic iron oxide nanoparticles (SPION) are potential drug carriers and a magnetic resonance imaging (MRI) contrast agent for cancer therapy and diagnosis.^[61]



14. Poly (ethylene oxide)-block-polyphosphoester-based paclitaxel conjugates as a platform for ultra-high paclitaxel-loaded multifunctional nanoparticles

Poly(ethylene oxide)-block-polyphosphoester-based paclitaxel conjugates as a platform for ultra-high paclitaxel-loaded multifunctional nanoparticles with high paclitaxel water solubility. A new type of degradable, nanoscopic polymer assembly containing ultra-high levels of drug loading via covalent attachment within amphiphilic core-shell nanoparticle morphology has been generated as a potentially effective and safe anti-cancer agent. Poly(ethylene oxide)-block-polyphosphoester-based paclitaxel drug conjugates (PEO-b-PPE-g-PTX) were synthesized by a rapid, scalable and versatile approach that involves only two steps: organocatalyst-promoted ring-opening-polymerization followed by click reaction-based conjugation of a PTX prodrug. Variations in the polymer-to-PTX stoichiometries allowed for optimization of the conjugation efficiency. The positive cell-killing activity of PEO-b-PPE-g-PTX against several cancer cell lines is demonstrated, and the presence of pendant reactive functionality provides a powerful platform for future work to involve conjugation of multiple drugs and imaging agents to achieve chemotherapy and bioimaging.^[62]

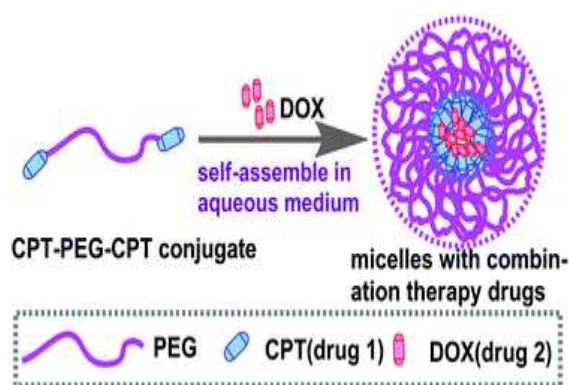


15. Intracellular cleavable poly(2-dimethylaminoethyl methacrylate) functionalized mesoporous silica nanoparticles for efficient siRNA delivery in vitro and in vivo

Intracellular cleavable poly(2-dimethylaminoethyl methacrylate) functionalized mesoporous silica nanoparticles exhibited low cytotoxicity and high siRNA delivery efficiency. A low cytotoxicity and high efficiency delivery system with the advantages of low cost and facile fabrication is needed for the application of small interfering RNA (siRNA) delivery both in vitro and in vivo.^[63]

16. Engineering of pegylated camptothecin into core-shell nanomicelles improving solubility, stability and combination delivery

PEGylated camptothecin nanomicelles were engineered with improved solubility, stability and capability of combination delivery. Camptothecin (CPT), a broad-spectrum anticancer drug, is limited in the extensive applications for its extremely hydrophobic property and low physiological stability in clinical use. In this study, prodrug of PEGylated CPT bioconjugate was synthesized to address the above critical issues. The as-designed amphiphilic conjugate could self-assemble into core-shell nanomicelles to enhance the solubility of the CPT and simultaneously improve the stability by encapsulating CPT in the micellar core.^[64]



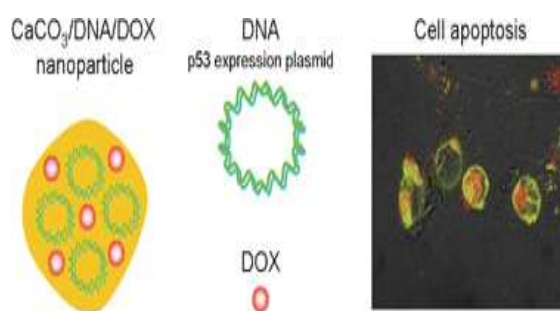
17. The use of a glucose-reduced graphene oxide suspension for photothermal cancer therapy

Photothermal cancer therapy using graphene oxide (GO) reduced by glucose in the presence of Fe (GRGO-Fe), hydrazine-reduced GO and CNTs. A single-step green method for effective reduction and functionalization of graphene oxide (GO) by glucose was developed. Then, efficacy of the glucose-reduced GO sheets in photothermal therapy of LNCaP prostate cancer cells was investigated *in vitro*. For complete destruction of the cancer cells at some time intervals of NIR irradiation (e.g., 0.5 and 12 min with a power density of 7.5 W cm^{-2}), minimum concentrations of the reduced GO sheets (i.e., 1 and 0.05 mg mL^{-1}) were obtained. The high photothermal therapy efficiency and biocompatibility of the glucose-reduced GO sheets were assigned to functionalization of the reduced sheets by gluconate ions which also prevented their aggregation. Review suggest that the glucose-reduced GO sheets can be used as biocompatible and efficient photothermal agents in upcoming nanotechnology-based cancer therapies without any common functionalization by polyethylene glycol.^[65]

17. Co-delivery of genes and drugs with nanostructured calcium carbonate for cancer therapy

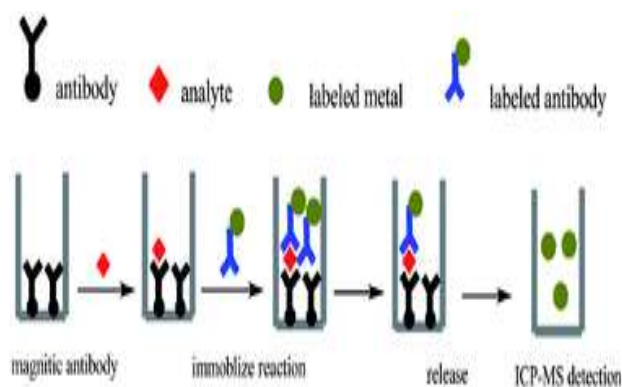
Nano-sized CaCO_3 /DNA/DOX co-precipitates for co-delivery of a p53 gene and a drug were prepared by a CaCO_3 co-precipitation technique. The CaCO_3 /DNA/DOX nanoparticles could effectively induce cell apoptosis and completely inhibit HeLa cell proliferation.

By using a CaCO_3 co-precipitation technique, p53 expression plasmids and doxorubicin hydrochloride (DOX) were encapsulated in nano-sized CaCO_3 /DNA/DOX co-precipitates for co-delivery of genes and drugs. Under a certain $\text{Ca}^{2+}/\text{CO}_3^{2-}$ ratio in the co-precipitation, both plasmid DNA and drugs could be loaded in the CaCO_3 /DNA/DOX nanoparticles with high encapsulation efficiency. The in vitro cell inhibition of the CaCO_3 /DNA/DOX nanoparticles was evaluated in HeLa cells by a MTT assay. The results showed the simultaneous treatment by gene and drug could induce cell apoptosis and completely inhibit the cell proliferation. The CaCO_3 /DNA/DOX nanoparticles exhibited a high cell inhibition rate of about 75%, indicating that the CaCO_3 /DNA/DOX nanoparticles could effectively mediate gene transfection and deliver the drug to the cells. Compared with the gene delivery system (CaCO_3 /DNA nanoparticles) or the free drug DOX, the co-delivery system (CaCO_3 /DNA/DOX nanoparticles) exhibits enhanced cell inhibition rate. The calcium carbonate based approach has great potential in the preparation of gene and drug co-delivery systems, and the CaCO_3 /DNA/DOX nanoparticles have promising applications in cancer treatment.^[66]



18. Magnetic quantitative immunoanalysis of carcinoembryonic antigen by ICP-MS with mercury labels

A novel nonisotopic immunoassay based on mercury labeled magnetic solid phase extraction-MCN-ICP-MS detection was proposed for the quantification of CEA.^[67]



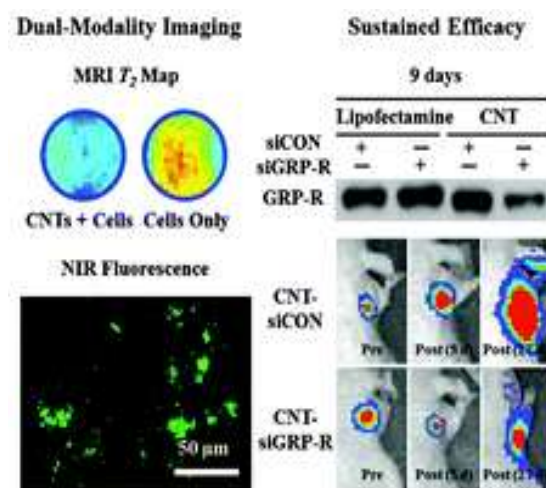
20. Multi trigger responsive, surface active lipid nanovesicle aerosols for improved efficacy of paclitaxel in lung cancer

The synergistic effect of multiple triggers (temperature and enzyme) towards improved efficacy of paclitaxel as nanovesicle aerosols. The present study focuses on the development of multi-trigger responsive surface active lipid nanovesicles encapsulating paclitaxel with the hypothesis that pulmonary surfactant mimetic lipid vesicles sensitive to temperature and enzyme simultaneously will offer synergistic advantage towards improved therapeutic efficacy of paclitaxel via aerosol administration. The nanovesicles showed a unimodal size distribution of the particles (100–150 nm) and high encapsulation efficiency of paclitaxel (82%). Triggered release of paclitaxel was observed at $\sim 42^{\circ}\text{C}$ in the presence of secretory phospholipase A_2 enzyme with maximum release observed with both the triggers used simultaneously. Since these nanovesicles are intended for aerosol administration in the treatment of lung cancer, they were engineered to have high surface activity and airway patency, in order to mimic pulmonary surfactant functions. Overall, these studies suggest the therapeutic potential and advantages of multi trigger responsive lipid nanovesicles with encapsulated paclitaxel over that of the commercially available form of paclitaxel namely Taxol, and suggests the feasibility of aerosol administration in the treatment of lung cancer and pulmonary metastasis.^[68]

21. Magneto-fluorescent carbon nanotube-mediated siRNA for gastrin- silencing releasing peptide receptor neuroblastoma

A magneto-fluorescent carbon nanotube-mediated siRNA system has been delivered to silence gastrin-releasing peptide receptor in neuroblastoma. We demonstrate a newly-developed magneto-fluorescent carbon nanotube (CNT)-mediated siRNA (CNT-siRNA) delivery system, which significantly silences our target of interest, gastrin-releasing peptide receptor (GRP-R), in neuroblastoma. CNT-siGRP-R resulted in a 50%

silencing efficiency and a sustained efficacy of 9 days for one-time siRNA treatment in vitro, whereas siRNA delivered by the commercial transfection reagent couldn't knockdown GRP-R expression. We further show that CNT-siRNA efficiently inhibits the growth of subcutaneous xenograft tumors in vivo.^[69]



22. Highly bioavailable anticancer herbal-loaded nanocarriers for use against breast and colon cancer in vitro and in vivo systems

This study focused on designing a large-scale producible vehicle for the pharmaceutically important compound berberine, to simultaneously improve its bioavailability against cancer cells and reduce cytotoxicity toward normal cells. This vehicle is composed of chitosan and tripolyphosphate, and was prepared with a simple ionic cross-linking method. The properties of the berberine-loaded chitosan-tripolyphosphate nanoparticles (BB-LCTNP) were dependent on berberine, chitosan, and tripolyphosphate concentrations. The bioavailability improvement and anticancer efficiency of the BB-LCTNPs were analyzed using MDA-MB-435 and Colo-205 cells. The results revealed that the particle size, loading efficiency, and IC_{50} of the BB-LCTNPs can be controlled easily. The pharmacodynamic availability of berberine increased up to 3 times when loaded into the nanoparticles because they directly targeted cancer cell nuclei. Moreover, the BB-LCTNPs were non-toxic toward normal cells. Studies revealed that BB-LCTNPs can reduce drug dosages up to 3 times and suppress tumor growth.^[70]

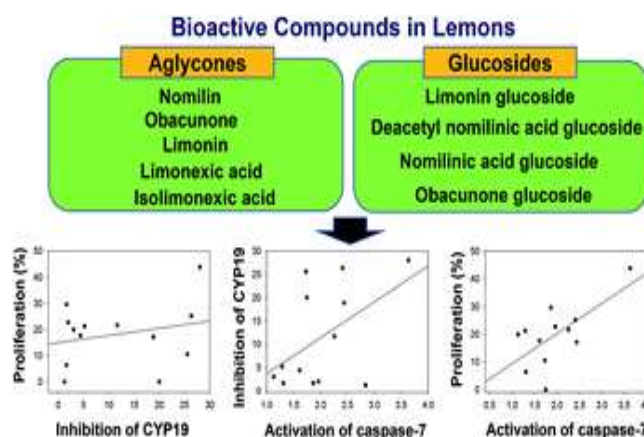
23. Ambient temperature synthesis of citrate stabilized and biofunctionalized, fluorescent calcium fluoride nanocrystals for targeted labeling of cancer cells

Highly fluorescent, citrate stabilized, biocompatible Eu^{3+} doped CaF_2 nanoparticles developed through aqueous chemistry routes, conjugated with anti-EGFR antibody

demonstrated efficient targeted labeling of EGFR over-expressing cancer cells. Targeted biological contrast agents are emerging as promising candidates in the field of cancer theragnostics. Herein, we report an ambient temperature synthesis of a nanosized, antibody functionalized lanthanide doped CaF_2 biolabel and demonstrate in vitro its potential for cancer cell targeting efficacy and specificity.^[71]

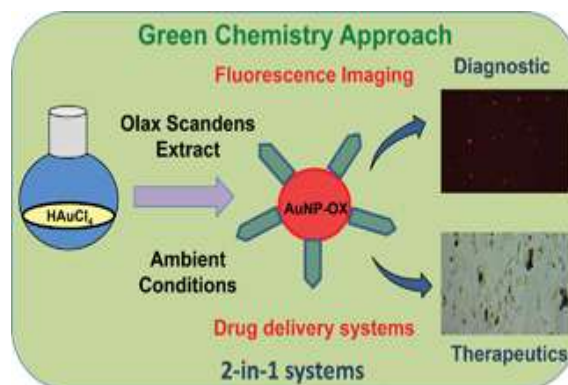
24. Limonoids and their anti-proliferative and anti-aromatase properties in human breast cancer cells

Lemons are a widely used citrus crop and have shown several potential health benefits. In the present study, the mechanism and effectiveness of the anti-cancer and anti-aromatase properties of limonoids were investigated for the first time. Our findings indicated that the citruslimonoids may have potential for the prevention of estrogen-responsive breast cancer.^[72]



25. Potential therapeutic and diagnostic applications of one-step in gold nanoconjugates (2-in-1 system) in cancer treatment.

An efficient, clean, fast and low cost green chemistry approach has been developed for the synthesis of gold nanoparticles using *Olax Scandens* leaf extract and their potential applications in cancer therapy. Synthesis of nanoparticles by a green chemistry approach has seen great attention due to several advantages compared to conventional chemical methods.^[73]



26. Phagocytes mediate targeting of iron oxide nanoparticles to tumors for cancer therapy

Phagocytes ingest nanoparticles and home to ovarian tumors, and this concentrates therapeutic nanoparticles in tumors after intraperitoneal injection of particles. Overall, the support IP injection of nanoparticles to utilize peritoneal phagocytes as a delivery vehicle in association with IONP-mediated hyperthermia as therapeutic strategies for ovarian and other peritoneal cancers.^[74]

27. Evidence for distinct mechanisms of uptake and antitumor activity of secretory phospholipase A₂ responsive liposome in prostate cancer

Over expression of secretory phospholipase A₂ and its receptors in tumors may be exploited to control drug delivery of liposomes. Secretory phospholipase A₂ (sPLA₂) cleave phospholipids at sn-2 ester bonds, releasing lysophospholipids and fatty acids, and are over expressed in several pathologies, including inflammation, arthritis, sepsis and breast and prostate cancers.^[75]

28. Immune stimulating photoactive hybrid nanoparticles for metastatic breast cancer

An engineered nanoparticle platform, which combines photodynamic therapy and the immune system for metastatic breast cancer. A therapeutic technology that combines the phototoxic and immune-stimulating ability of photodynamic therapy (PDT) with the widespread effectiveness of the immune system can be very promising to treat metastatic breast cancer.^[76]

29. Real-time impedance analysis of silica nanowire toxicity on epithelial breast cancer cells

It demonstrates dynamic, multi-spatial, impedance measurements to evaluate the effect of silica nanowires on Hs578T epithelial breast cancer cells.^[77]

30. Cytotoxicity and slow release of the anti-cancer drug doxorubicin from ZIF-8

The antitumoral potential and cytotoxicity of the doxorubicin-ZIF-8 (DOXO-ZIF-8) complex towards the mucoepidermoid carcinoma of human lung (NCI-H292), human colorectal adenocarcinoma (HT-29), and human promyelocytic leukemia (HL-60) cell lines.^[78]

Nanotechnology in Cancer: Advantages & Disadvantages

Advantages

- Reduce side effects of chemotherapy drugs by using nanoparticles to deliver the drugs directly to the tumor and avoid interaction with healthy tissue.
- Allows early detection of cancer by using antibodies covered in nanoparticles that bind to cancerous cells and light them up.
- Avoids destroying healthy cells by destroying tumors from within using nanoshells.
- Determine stage of cancer using cantilevers to detect concentration of cancer cells.
- Detect the presence of altered genes that cause cancer using nanowires.

Disadvantages

- Potential toxicity of nanomaterial could cause tissue damage.
- The size and high reactivity properties of nanomaterials could have implications on the environment, health and safety.
- Nanotechnology could be used irresponsibly and potentially cause health and environmental problems.
- Lack of knowledge of the effects of nanotechnology on the nanoscale.
- May not be possible to produce mass forms of nanotechnology.

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