Health, 2015, 7, 580-588
Published Online May 2015 in SciRes. http://www.scirp.org/journal/health
http://dx.doi.org/10.4236/health.2015.75069

Prostate Cancer's Molecular Imaging by Targeting Based Nanoparticles: An Overview

Hossein Heidari[1*], Alireza Salehi Fordoei[1,2*], Mostafa Saffary[3], Mehdi Shafiee Ardestani[4#]

[1]Department of HIV and Hepatitis B, Pasteur Institute of Iran, Tehran, Iran
[2]Blood Transfusion Organization, Qom, Iran
[3]Addiction Research Department, Kashan University of Medical Sciences, Kashan, Iran
[4]Department of Radio-Pharmacy, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran
Email: [#]shafieeardestani@gmail.com, [#]shafieeardestani@sina.tums.ac.ir

Received 28 December 2014; accepted 17 May 2015; published 20 May 2015

Abstract

Today nanoparticles based drug delivery or imaging agents are extremely being investigated as a very powerful tool in early diagnostics or treatment of different kinds of cancers including prostate malignancies. Among the diverse developing nanomaterials, biocompatible biodegradable dendrimers and chitosan or PLGA (Poly Lactic-co-Glycolic Acid) derivatives are more considered due to their safer profiles. As a result, finding novel prostate imaging agents based on nano sized structures would be of high global interest which will be further discussed in this review.

Keywords

PLGA, Dendrimer, Nanoparticles Based Drug Delivery or Imaging Agents, Prostate Malignancies

1. Introduction

Molecular imaging is an emerging and exciting ongoing area in the field of radiological sciences including all imaging instrumental applications such as PET, SPECT or MRI, and pharmaceutical sciences as well including but not limited to radiopharmaceutical sciences and nano-pharmaceutics to produce novel manipulated nano biomaterials to help physicians better understand the disease problems or follow up the treatment response. PET or SPECT radiopharmaceuticals have costly production and imaging procedure, time dependent behavior, radiations half-life which can be hazardous to medical staff and patients. However, they have much better characteristics and higher imaging quality compared with the above MRI radiopharmaceuticals. Traditional MRI con-

[*]These two authors contributed in this study equally.
[#]Corresponding author.

How to cite this paper: Heidari, H., Fordoei, A.S., Saffary, M. and Ardestani, M.S. (2015) Prostate Cancer's Molecular Imaging by Targeting Based Nanoparticles: An Overview. *Health*, **7**, 580-588. http://dx.doi.org/10.4236/health.2015.75069

trast agents like Magnevist (Gadopentate dimeglumine) and Omni scan (Gadodiamide) are classified as extracellular fluid imaging contrast agents and do not able to penetrate to intracellular spaces as well. In spite, recent efforts attempted to design and develop novel molecular contrast media imaging agents to overcome the extracellular imaging defaults [1]-[11] (see **Figure 1** and **Figure 2**) [12].

As a result, finding novel prostate imaging agents based on nano sized structures would be of high global interest which will be further discussed in this review.

In engineering science, a particle is outlined as a little object that behaves as a full unit with relation to its transport and properties. Particles are additionally classified in keeping with diameter [1]. Coarse particles have a diameter ranging between 500 and 10,000 nanometers. Fine particles are sized between one hundred and a couple of, 500 nanometers. Ultrafine particles, or nanoparticles, are between one and one hundred nanometers in size. Nanoparticle characterization is important to ascertain understanding and management of nanoparticle synthesis and applications. Characterization is completed by employing a style of totally different techniques, primarily drawn from materials science. Common techniques are microscopy (TEM, SEM), atomic force research (AFM), dynamic lightweight scattering (DLS), X-ray negatron spectroscopic analysis (XPS), powder X-ray diffraction (XRD), Fourier rework infrared spectroscopic analysis (FTIR), matrix-assisted optical device desorption/ionization time-of-flight mass spectroscopy (MALDI-TOF), ultraviolet-visible spectroscopic analysis, twin polarization interferometry and nuclear resonance (NMR).

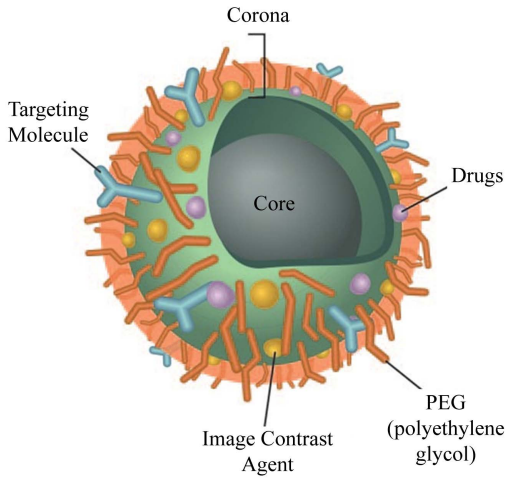

Figure 1. Multifunctional nanoparticle. The nanoparticle's "corona" can be functionalized with hydrophilic polymers, targeting molecules, therapeutic Drugs, and image contrast agents. The interior core can be solid (e.g., quantum dots) or liquid (e.g., liposomes). Molecules are not shown to scale. PEG, polyethylene glycol.

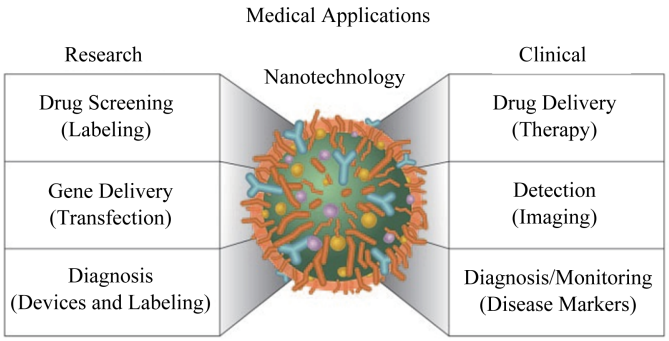

Figure 2. Medical applications of nanotechnology. The size and tailorability of nanoparticles may lead to their widespread use in a variety of medical applications.

While the speculation has been well known for over a century (see Henry M. Robert Brown), the technology for nanoparticle pursuit analysis (NTA) permits direct pursuit of the Brownian motion. This methodology, therefore, permits the filler of individual nanoparticles in answer.

2. PLGA

PLGA or poly (lactic-co-glycolic acid) could be a polymer that is employed during a host of Food and Drug Administration (FDA) approved therapeutic devices, thanks to its biodegradability and biocompatibility. PLGA is synthesized by means that of random ring-opening co-polymerization of 2 totally different monomers, the cyclic dimers (1, 4-dioxane-2, 5-diones) of acid and carboxylic acid. Common catalysts utilized in the preparation of this chemical compound embrace tin (II) 2-ethylhexanoate, tin (II) alkoxides, or aluminium isopropoxide. Throughout polymerization, serial monomeric units (of glycolic or potable acid) are joined along in PLGA by organic compound linkages, therefore yielding a linear, acyclic polyester as a product [1].

PLGA has been self-made as a perishable chemical compound as a result of it undergoes chemical reaction within the body to supply the first monomers, carboxylic acid and acid. These 2 monomers beneath traditional physiological conditions, are by-products of assorted metabolic pathways within the body. Since the body effectively deals with the 2 monomers, there's tokenish general toxicity related to mistreatment PLGA for drug delivery or biomaterial applications. Also, the chance to tailor the chemical compound degradation time by fixing the quantitative relation of the monomers used throughout synthesis has created PLGA a standard selection within the production of a spread of medical specialty devices, such as, grafts, sutures, implants, prosthetic devices, surgical sealing material films, small and nanoparticles. Specific samples of use include:

- Successful within the delivery of Polymox for the treatment infectious disease (treatment of L. monocytogenes infection).
- A commercially obtainable drug delivery device mistreatment PLGA is Lupron Depot for the treatment of advanced glandular carcinoma.
- Prophylactic delivery of the antibiotic drug into the central system nervous once applied to the surface of the brain when brain surgery [2].

3. Chitosans

Chitosan could be a linear sugar composed of arbitrarily distributed β-(1-4)-linked D-glucosamine (deacetylated unit) and N-acetyl-D-glucosamine (acetylated unit). It's created by treating shrimp and alternative crustacean shells with the alkali hydrated oxide.

Chitosan is created commercially by deacetylation of polysaccharide that is that the structural part within the body covering of crustaceans (such as crabs and shrimp) and cell walls of fungi. The degree of deacetylation (%DD) is determined by proton magnetic resonance spectroscopic analysis, and therefore to feature in business chitosans ranges from sixty to 100 percent. On average, the relative molecular mass of commercially created chitosan is between 3800 and 20,000 Daltons. A standard methodology for the synthesis of chitosan is that the deacetylation of polysaccharide mistreatment hydrated oxide in excess as a chemical agent and water as a solvent. This reaction pathway, once allowed to travel to completion (complete deacetylation) yields up to ninety eight product [2].

Chitosan's properties permit it to apace clot blood, and has recently gained approval within the U.S. and Europe to be used in bandages and alternative astringent agents. Chitosan astringent product are shown in testing by the U.S. United States Marines to quickly stop hemorrhage and to cut back blood loss, and end in 100 percent survival of otherwise deadly blood vessel wounds in artiodactyl [13]. Chitosan astringent product scale back blood loss compared to gauze dressings and increase patient survival [14]. Chitosan astringent product are sold-out to the U.S. Army and are presently employed by the United Kingdom military. Each the North American country and kingdom have already used the bandages on the battlefields of Asian country and Islamic State of Afghanistan [15]. Chitosan is hypoallergenic and has natural medication properties, that additional support its use in field bandages [3]-[9].

Chitosan's properties additionally permit it to be utilized in stratum drug delivery; it's mucoadhesive in nature, reactive (so it is created in many alternative forms), and most significantly, contains an electric charge beneath acidic conditions. This electric charge comes from protonation of its free amino teams. Lack of an electric charge means that chitosan is insoluble in neutral and basic environments. However, in acidic environments,

protonation of the amino teams ends up in a rise in solubility. The implications of this are vital to medical specialty applications. This molecule can maintain its structure during a neutral atmosphere, however can solubilize associate degreed degrade in an acidic atmosphere. This implies chitosan is accustomed transport a drug to associate degree acidic atmosphere, wherever the chitosan packaging can then degrade, cathartic the drug to the specified atmosphere [16]. One example of this drug delivery has been the transport of internal secretion [17].

4. Dendrimers

Dendrimers are repetitively branched molecules [1] [2]. Dendritic molecules are characterized by structural perfection. Dendrimers and dendrons are monodisperse and frequently extremely stellate, spherical compounds. The sphere of nerve fiber molecules is roughly divided into low-molecular weight and high-molecular weight species. The primary class includes dendrimers and dendrons, and therefore the latter includes dendronized polymers, hyper branched polymers, and therefore the chemical compound brush.

The properties of dendrimers are dominated by the useful teams on the molecular surface, however, there are samples of dendrimers with internal practicality [1]-[10] [18]-[21]. Nerve fiber encapsulation of useful molecules permits for the isolation of the site, a structure that mimics that of active sites in biomaterials [22]-[24]. Additionally, it's potential to form dendrimers water soluble, in contrast to most polymers, by functionalizing their outer shell with charged species or alternative deliquescent teams. Alternative governable properties of dendrimers embrace toxicity, crystallinity, tecto-dendrimer formation, and chirality [22]-[31].

Applications of dendrimers usually involves conjugating alternative chemical species to the dendrimer surface that may perform as sleuthing agents (such as a dye molecule), affinity ligands, targeting elements, radio ligands, imaging agents, or pharmaceutically active compounds. Dendrimers have terribly sturdy potential for these applications as a result of their structure will cause multivalent systems. In alternative words, one dendrimer molecule has many potential sites to couple to a lively species. Researchers aimed to utilize the hydrophobic environments of the nerve fiber media to conduct chemical science reactions that generate the product that are synthetically challenged. Acid and phenol terminated water soluble dendrimers were synthesized to ascertain their utility in drug delivery in addition as conducting chemical reactions in their interiors [32]. This may permit researchers to connect each targeting molecules and drug molecules to a similar dendrimer, that may scale back negative facet effects of medicines on healthy cells [26].

4.1. Liposomes

Liposomes are usually composed of phosphatidylcholine-enriched phospholipids and should additionally contain mixed super molecule chains with wetter properties like egg phosphatidylethanolamine. A cyst style could use surface ligands for attaching to unhealthy tissue [1]. The major styles of liposomes are the multilamellar cyst (MLV), the tiny unilamellar cyst (SUV), the massive unilamellar cyst (LUV), and therefore the cochlea cyst [31] [33]-[37].

Liposomes shouldn't be confused with micelles and reverse micelles composed of monolayers further advances in cyst analysis are ready to permit liposomes to avoid detection by the body's system, specifically, the cells of RES (RES). These liposomes are referred to as "stealth liposomes", and are created with PEG (Polyethylene Glycol) studding the skin of the membrane. The PEG coating, that is inert within the body, permits for extended circulatory life for the drug delivery mechanism. However, analysis presently seeks to research at what quantity of PEG coating the PEG really hinders binding of the cyst to the delivery website. Additionally to a PEG coating, most stealing cysts even have some style of biological species hooked up as a matter to the liposome so as to change binding via a selected expression on the targeted drug delivery website. These targeting ligands might be being associate degreetibodies (making an immunoliposome), vitamins, or specific antigens. Targeted liposomes will target nearly any cell kind within the body and deliver medication that might naturally be systemically delivered. Naturally harmful medication is a lot of less harmful if delivered solely to pathologic tissues. Polymersomes, morphologically associated with liposomes, can even be used this manner.

4.2. Iron Chemical Compound Nanoparticles

Iron chemical compound nanoparticles are iron chemical compound particles with diameters between regarding one and one hundred nanometers. The 2 main types are magnetic iron-ore (Fe_3O_4) and its oxidized form maghemite (γ-Fe_2O_3). Magnetite has associate degree inverse mineral structure with element forming a face-centered

cube like crystal system. In magnetic iron-ore, all tetrahedral sites are occupied by Fe^{3+} and octahedral sites are occupied by each Fe^{3+} and Fe^{2+}.

Maghemite differs from magnetic iron-ore in this all or most of the iron is within the powerfulness state (Fe^{3+}) and by the presence of ion vacancies within the octahedral sites. Maghemite contains a cube like unit within which every cell contains thirty two O ions, 211/3 Fe^{3+} ions and 22/3 vacancies. The cations are distributed arbitrarily over the eight tetrahedral and sixteen octahedral sites due to its four mismatched electrons in 3d shell, associate degree iron atom contains a sturdy torsion.

Ions Fe^{2+} have additionally four mismatched electrons in 3d shell and Fe^{3+} have five mismatched electrons in 3d shell. Therefore, once crystals are shaped from iron atoms or ions Fe^{2+} and Fe^{3+} they can be in magnetic force, magnetic attraction or ferromagnetic states.

In the magnet state, the individual atomic magnetic moments are arbitrarily familiarized, and therefore the substance contains a zero internet torsion if there's no field of force. These materials have a relative magnetic permeableness larger than one and are interested in magnetic fields. The torsion drops to zero once the applied field is removed. However during a magnetic force material, all the atomic moments are aligned even while not associate degree external field. A ferromagnetic material is comparable to a ferromagnet however has 2 differing types of atoms with opposing magnetic moments. The fabric contains a torsion as a result of the opposing moments have totally different strengths. If they need a similar magnitude, the crystal is magnetic attraction and possesses no internet torsion [3].

Magnetite and maghemite are most well-liked in biomedicine as a result of they're biocompatible and doubtless non-toxic to humans [38]. Iron chemical compound is well degradable and thus helpful for *in vivo* applications [39]. Results from exposure of somebody's epithelial tissue cell line and a murine embryonic cell line to seven industrially necessary nanoparticles showed a nanoparticle specific cytotoxic mechanism for uncoated iron chemical compound [7]. Solubility was found to powerfully influence the cytotoxic response. Labelling cells (e.g. stem cells, nerve fiber cells) with iron chemical compound nanoparticles is a stimulating new tool to observe such tagged cells in real time by resonance imaging [8] (see **Table 1**).

4.3. Contrast Agents

A medical medium (or distinction agent) could be a substance accustomed enhance the distinction of structures or fluids among the body in medical imaging [1]. It's ordinarily accustomed enhance the visibility of blood vessels and therefore the digestive tract.

Several styles of distinction media are in use in medical imaging and that they will roughly be classified supported the imaging modalities wherever they're used. Though alternative sorts exist, most typical distinction agents work supported X-ray attenuation and resonance signal sweetening. Iodine and atomic number 56 are the foremost common styles of medium for enhancing X-ray-based imaging strategies. Varied kinds of element distinction media exist, with variations occurring between the osmolarity, consistency and absolute iodine content of various media. Non-ionic dimers are favored for his or her low osmolarity and toxicity, however have a correspondingly higher value hooked up to their use [2].

4.4. Magnetic Resonance Imaging Distinction Agent

This would embrace atomic number 64 to be used in resonance imaging as a magnetic resonance imaging distinction agent. Within the 3+ number the metal has seven mismatched electrons. This causes water round the distinction agent to relax quickly, enhancing the standard of the magnetic resonance imaging scan.

Table 1. Example of nanoparticles used in biological research.

Nanoparticle	Application	Reference
Dendrimers	Targeting of cancer cells, drug delivery, imaging, boron neutron capture therapy	[13]-[15] [40]
Liposomes	Specific targeting of cancer cells, gene therapy, drug delivery	[41]-[43]
Poly lactic-co-glycolic acid (PLGA)	Targeting of cancer cells, drug delivery, cancer vaccine, treatment	[16] [17] [44] [45]
Chitosan	Imaging and therapy, targeting	[46] [47]
Micelles	Targeting, imaging, drug delivery	[48]-[50]

4.5. Nuclear Molecular Imaging Modalities

Single-photon emission computed tomography (SPECT) is a nuclear medicine tomographic imaging technique using gamma rays. It is very similar to conventional nuclear medicine planar imaging using a gamma camera. However, it is able to provide true 3D information. This information is typically presented as cross-sectional slices through the patient, but can be freely reformatted or manipulated as required.

Positron emission tomography (PET) is a nuclear medicine, functional imaging technique that produces a three-dimensional image of functional processes in the body. The system detects pairs of gamma rays emitted indirectly by a positron-emitting radionuclide (tracer), which is introduced into the body on a biologically active molecule. Three-dimensional images of tracer concentration within the body are then constructed by computer analysis [51].

4.6. Prostate Cancer, Nanoparticles and Molecular Imaging

Prostate cancer is that the most typical malignancy among men, accounting for 100 percent of all cancer-related deaths in 2008 [1].

Typical imaging, which has computed tomography (CT), magnetic resonance Imaging (MRI), and ultrasound, is presently accustomed detect organ-confined or pathologic process unwellness for staging and decisive prognosis.

However, there is substantial area for improvement within the specificity and sensitivity of imaging for detecting little primary lesions and for distinctive tokenish, pathologic process unwellness [2].

At present, a spread of nanoparticle systems are being investigated to explore their potential in molecular imaging, with several applications aimed toward diagnosing or treatment of cancer [9].

Particle charge, size, form and hydrophilicity stay among the foremost necessary properties of nanoparticles for effective delivery to the specified target. synthetic resin glycol (PEG) molecules are investigated extensively as a good means that to supply deliquescent “stealth” properties, ordinarily yielding reduced nonspecific sorption of blood serum proteins *in vivo*, therefore manufacturing longer circulation times [32] [37] [52]-[54]. Conversely, charged nanoparticles are being designed for enhancing endocytosis or activity for cell labeling [18].

Varied styles of nanoparticle are currently beneath investigation, as well as solid super molecule nanoparticles, liposomes, micelles, nanotubes, gilded nanoparticles, quantum dots, dendrimers, compound nanoparticles and element nanoparticles. This review primarily emphasizes four representative nanomaterials (gold nanoparticles, quantum dots, iron oxide nanoparticles and dendrimers) in medical specialty imaging applications. There’s additionally a quick discussion on alternative sundry nanoparticles.

Magnetic resonance imaging (MRI) and resonance spectroscopic analysis (MRS) are employed within the detection and characterization of glandular carcinoma.

Despite the connexion of PSMA in glandular carcinoma, Prostascint (Cytogen, Princeton, NJ), a radiolabeled protein targeted to the PSMA, has been found to own many important shortcomings, as well as restricted prognosticative worth in imaging the prostate fossa, significantly following actinotherapy, and low sensitivity for sleuthing osteal metastases; Prostascint is also technically tightened and needs interpretation at sites with expertise and expertise [41].

Recently, investigators from Johns Hopkins University given the preparation of radiolabeled small-molecule ligands for PSMA ([125I]DCIT, [11C]DCMC, [18F]DCFBC], in addition as seven Tc 99m- or rhenium-labeled chelating agents attached to associate degree amino-functionalized PSMA matter with or while not a variable length linker moiety [42]-[44]. These efforts were supported potential capitalization on PSMA as a relevant biologic target for imaging and medical care of glandular carcinoma.

Positron emission imaging (PET) with [18F]-fluorodeoxyglucose (FDG) could be a molecular imaging technique that monitors tissue aldohexose metabolism, taking advantage of the long known phenomenon that the majority tumors are hyper metabolic with exaggerated aldohexose metabolism (Warburg effect). The up regulation of aldohexose transporter (GLUT) proteins Engineered mouse models of glandular carcinoma are developed in conjunction with imaging markers to permit *in vivo* observance of tumour growth at totally different stages of the disease and to facilitate the interpretation of the mouse studies into human clinical trials.

5. Conclusions

A key challenge within the development of “smart” molecular targeted tools for medical specialty imaging is the

capability for selective attachment and representing multiple functionalities on the nanoparticle platform.

References

[1] Lin, W., *et al*. (2009) Magnetic Nanoparticles for Early Detection of Cancer by Magnetic Resonance Imaging. *MRS Bulletin*, **34**, 441-448. http://dx.doi.org/10.1557/mrs2009.120

[2] Sun, C., *et al*. (2008) Magnetic Nanoparticles in MR Imaging and Drug Delivery. *Advanced Drug Delivery Reviews*, **60**, 1252-1265. http://dx.doi.org/10.1016/j.addr.2008.03.018

[3] Reddy, J.M. and Prasad, V. (2005) Step by Step MRI. 3rd Edition, Jaypee Brothers, New Delhi, 124-125. http://dx.doi.org/10.5005/jp/books/10844

[4] Sasaki, M., *et al*. (2005) Enhancement Effects and Relaxivities of Gadolinium-DTPA at 1.5 versus 3 Tesla: A Phantom Study. *Magnetic Resonance in Medical Sciences*, **4**, 145-149. http://dx.doi.org/10.2463/mrms.4.145

[5] Raymond, K.N. and Pierre, V.C. (2005) Next Generation, High Relaxivity Gadolinium MRI Agents. *Bioconjugate Chemistry*, **16**, 3-8. http://dx.doi.org/10.1021/bc049817y

[6] Moriggi, L.C. (2009) Gold Nanoparticles Functionalized with Gadolinium Chelates as High-Relaxivity MRI Contrast Agents. *Journal of the American Chemical Society*, **131**, 10828-10829. http://dx.doi.org/10.1021/ja904094t

[7] Wai-Yan, C. and Wing-Tak, W. (2007) Small Molecular Gadolinium (III) Complexes as MRI Contrast Agents for Diagnostic Imaging. *Coordination Chemistry Reviews*, **251**, 2428-2451. http://dx.doi.org/10.1016/j.ccr.2007.04.018

[8] Shahbazi-Gahrouei, D., *et al*. (2001) *In Vivo* Studies of Gd-DTPA-Monoclonal Antibody and Gd-Porphyrins: Potential Magnetic Resonance Imaging Contrast Agents for Melanoma. *Journal of Magnetic Resonance Imaging*, **14**, 169-174. http://dx.doi.org/10.1002/jmri.1168

[9] Amanluo, M., *et al*. (2011) Gd^{3+}-DTPA-DG: Novel Nanosized Dual Anticancer and Molecular Imaging Agent. *International Journal of Nanomedicine*, **6**, 747-763.

[10] Ananta, J.S., *et al*. (2010) Geometrical Confinement of Gadolinium-Based Contrast Agents in Nanoporous Particles Enhances T_1 Contrast. *Nature Nanotechnology*, **5**, 815-821. http://dx.doi.org/10.1038/nnano.2010.203

[11] Shahbazi-Gahrouei, D., Roufeh, M. and Tavakoli, M.B. (2006) Gadolinium-Diethylenetriaminepenta-Acetic Acid Conjugated with Monoclonal Antibody C595 as New Magnetic Resonance Imaging Contrast Agents for Breast Cancer (MCF-7) Detection. *Iranian Biomedical Journal*, **10**, 209-213.

[12] McNeil, S.E. (2005) Nanotechnology for the Biologist. *Journal of Leukocyte Biology*, **78**, 585-594. http://dx.doi.org/10.1189/jlb.0205074

[13] Dubey, P.K., Mishra, V., Jain, S., Mahor, S. and Vyas, S.P. (2004) Liposomes Modified with Cyclic RGD Peptide for Tumor Targeting. *Journal of Drug Targeting*, **12**, 257-264. http://dx.doi.org/10.1080/10611860410001728040

[14] Vandamme, T.F. and Brobeck, L. (2005) Poly(Amidoamine) Dendrimers as Ophthalmic Vehicles for Ocular Delivery of Pilocarpine Nitrate and Tropicamide. *Journal of Controlled Release*, **102**, 23-38. http://dx.doi.org/10.1016/j.jconrel.2004.09.015

[15] Yang, W., Barth, R.F., Wu, G., Bandyopadhyaya, A.K., Thirumamagal, B.T., Tjarks, W., Binns, P.J., Riley, K., Patel, H., Coderre, J.A., Ciesielski, M.J. and Fenstermaker, R.A. (2004) Boronated Epidermal Growth Factor as a Delivery Agent for Neutron Capture Therapy of EGF Receptor-Positive Gliomas. *Applied Radiation and Isotopes*, **61**, 981-985. http://dx.doi.org/10.1016/j.apradiso.2004.05.071

[16] Hamedy, S., Haddadi, A., Hung, R.W. and Lavasanifar, A. (2011) Targeting Dendritic Cells with Nano-Particulate PLGA Cancer Vaccine Formulation. *Advance Drug Delivery Reviews*, **63**, 943-955. http://dx.doi.org/10.1016/j.addr.2011.05.021

[17] Hasan, W., Chu, K., Gullapalli, A., Dunn, S.S., Enlow, E.M., Luft, J.C., Tian, S.M., Napier, M.E., Pohlhaus, P.D., Rolland, J.P. and DeSimone, J.M.(2012). Delivery of Multiple siRNAs Using Lipid-Coated PLGA Nanoparticles for Treatment of Prostate Cancer. *Nano Letters*, **12**, 287-292. http://dx.doi.org/10.1021/nl2035354

[18] Burtea, C., Laurent, S., Colet, J.M., Vander, E.L. and Muller, R.N. (2003) Development of New Glycosylated Derivatives of Gadolinium Diethylenetriaminepentaacetic for Magnetic Resonance Angiography. *Investigative Radiology*, **38**, 320-333. http://dx.doi.org/10.1097/01.RLI.0000066251.65982.e6

[19] Ganapathy, V., Thangaraju, M. and Prasad, P.D. (2009) Nutrient Transporters in Cancer: Relevance to Warburg Hypothesis and Beyond. *Pharmacology & Therapeutics*, **121**, 29-40. http://dx.doi.org/10.1016/j.pharmthera.2008.09.005

[20] Ardestani, M.S., *et al.* (2010) Novel and Facile Methods for the Synthesis of DTPA-Mono-Amide: A New Completely Revised Strategy in Radiopharmaceutical Chemistry. *Journal of Radioanalytical and Nuclear Chemistry*, **283**, 447-455. http://dx.doi.org/10.1007/s10967-009-0414-y

[21] Shen, Z.Y., Li, Y., Kohama, K., Oneill, B. and Bi, J.X. (2011) Improved Drug Targeting of Cancer Cells by Utilizing

Actively Targetable Folic Acid-Conjugated Albumin Nanospheres. *Pharmacological Research*, **63**, 51-58. http://dx.doi.org/10.1016/j.phrs.2010.10.012

[22] Li, L.L., Yin, Q., Cheng, J.J. and Lu, Y. (2012) Polyvalent Mesoporous Silica Nanoparticle-Aptamer Bioconjugates Target Breast Cancer Cells. *Advanced Healthcare Materials*, **1**, 567-572. http://dx.doi.org/10.1002/adhm.201200116

[23] de la Fuente, J.M. and Penadés, S. (2006) Glyconanoparticles: Types, Synthesis and Applications in Glycoscience, Biomedicine and Material Science. *Biochimica et Biophysica Acta*, **1760**, 636-651.

[24] Veerapandian, M. and Yun, K. (2010) Synthesis of Silver Nanoclusters and Functionalization with Glucosamine for Glyconanoparticles. *Synthesis and Reactivity in Inorganic, Metal-Organic, and Nano-Metal Chemistry*, **40**, 56-64.

[25] Rojo, J., *et al*. (2004) Gold Glyconanoparticles as New Tools in Antiadhesive Therapy. *ChemBioChem*, **5**, 291-297. http://dx.doi.org/10.1002/cbic.200300726

[26] Mirzaei, M., *et al*. (2012) Novel Nanosized Gd^{3+}-ALGD-G_2-C595: *In Vivo* Dual Selective MUC-1 Positive Tumor Molecular MR Imaging and Therapeutic Agent. *Journal of Nanomedicine Nanotechnology*, **3**, 1-6. http://dx.doi.org/10.4172/2157-7439.1000147

[27] Mirzaei, M., *et al*. (2012) Gd^{3+}-Anionic Linear Globular Dendrimer-G_2-C595 a Dual Novel Nanoprobe for MR Imaging and Therapeutic Agent: An *in Vitro* Study. *Biomolecular Research & Therapeutics*, **1**, 103.

[28] Bayly, S.R., Fisher, C.L., Storr, T., Adam, M.J. and Orvig, C. (2004) Carbohydrate Conjugates for Molecular Imaging and Radiotherapy: ^{99m}Tc(I) and ^{186}Re(I) Tricarbonyl Complexes of N-(2'-Hydroxybenzyl)-2-amino-2-deoxy-D-glucose. *Bioconjugate Chemistry*, **15**, 923-926. http://dx.doi.org/10.1021/bc0499681

[29] Mehravi, B., *et al*. (2013) Facile Conjugation of Glucosamine on Gd^{3+} Based Nanoporous Silica Using Heterobifunctional Crosslinker (ANB-NOS) for Cancer Cell Imaging. *International Journal of Nanomedicine*, **8**, 3383-3394. http://dx.doi.org/10.2147/IJN.S44829

[30] Mehravi, B., *et al*. (2013) Cellular Uptake and Imaging Studies of Glycosylated Silica Nanoprobe (GSN) in Human Colon Adenocarcinoma (HT 29 Cell Line). *International Journal of Nanomedicine*, **8**, 3209-3216. http://dx.doi.org/10.2147/IJN.S44815

[31] Schibli, R., Dumas, C., *et al*. (2005) Synthesis and *in Vitro* Characterization of Organometallic Rhenium and Technetium Glucose Complexes against Glut 1 and Hexokinase. *Bioconjugate Chemistry*, **16**, 105-112. http://dx.doi.org/10.1021/bc049774l

[32] Taylor, R.A., Phelan, P.E., Otanicar, T.P., Adrian, R. and Prasher, R. (2011) Nanofluid Optical Property Characterization: Towards Efficient Direct Absorption Solar Collectors. *Nanoscale Research Letters*, **6**, 225. http://dx.doi.org/10.1186/1556-276X-6-225

[33] Ardestani, M.S. (2010) Potential Opponent for 18FDG: Gd^{3+}-DTPA-DG: A New Synthetic MRI Contrast Agent. *Iranian Journal of Radiology*, **7**, 56.

[34] Mehravi, B., *et al*. (2014) Breast Cancer Cells Imaging By Targeting Methionine Transporters with Gadolinium-Based Nanoprobe. *Molecular Imaging and Biology*, **16**, 519-528. http://dx.doi.org/10.1007/s11307-014-0718-3

[35] Darvish, M.T., *et al*. (2013) Gd^{3+}-DTPA-Meglumine-Anionic Linear Globular GI: Novel Nanosized Law Toxic Tumor Molecular MR Imaging Agent. *ISRN Pharmaceutics*, **2013**, Article ID: 378452.

[36] Dabbs, D.M. and Aksay, I.A. (2000) Self-Assembled Ceramics Produced by Complex-Fluid Templation. *Annual Review of Physical Chemistry*, **51**, 601-622. http://dx.doi.org/10.1146/annurev.physchem.51.1.601

[37] Buffat, Ph. and Borel, J.-P. (1976) Size Effect on the Melting Temperature of Gold Particles. *Physical Review A*, **13**, 2287. http://dx.doi.org/10.1103/PhysRevA.13.2287

[38] Carretero, M.I. and Pozo, M. (2009) Clay and Non-Clay Minerals in the Pharmaceutical Industry: Part I. Excipients and Medical Applications. *Applied Clay Science*, **46**, 73-80.

[39] Park, J., Cho, W., Park, H.J., Cha, K.H., Ha, D.C., Choi, Y.W., Lee, H.Y., Cho, S.H. and Hwang, S.J. (2013) Biodistribution of Newly Synthesized PHEA-Based Polymer-Coated SPION in Sprague Dawley Rats as Magnetic Resonance Contrast Agent. *International Journal of Nanomedicine*, **8**, 4077-4089.

[40] Quintana, A., Raczka, E., Piehler, L., Lee, I., Myc, A., Majoros, I., Patri, A.K., Thomas, T., Mule, J. and Baker Jr., J.R. (2002) Design and Function of a Dendrimer-Based Therapeutic Nanodevice Targeted to Tumor Cells through the Folate Receptor. *Pharmaceutical Research*, **19**, 1310-1316. http://dx.doi.org/10.1023/A:1020398624602

[41] Dubey, P.K., Mishra, V., Jain, S., Mahor, S. and Vyas, S.P. (2004) Liposomes Modified with Cyclic RGD Peptide for Tumor Targeting. *Journal of Drug Targeting*, **12**, 257-264. http://dx.doi.org/10.1080/10611860410001728040

[42] Reszka, R.C., Jacobs, A. and Voges, J. (2005) Liposome-Mediated Suicide Gene Therapy in Humans. *Methods in Enzymology*, **391**, 200-208. http://dx.doi.org/10.1016/S0076-6879(05)91012-4

[43] ten Hagen, T.L. (2005) Liposomal Cytokines in the Treatment of Infectious Diseases and Cancer. *Methods in Enzymology*, **391**, 125-145. http://dx.doi.org/10.1016/S0076-6879(05)91007-0

[44] Thamake, S.I., Raut, S.L., Gryczynski, Z., Ranjan, A.P. and Vishwanatha, J.K. (2012) Alendronate Coated Poly-Lactic-Co-Glycolic Acid (PLGA) Active Targeting of Metastatic Breast Cancer. *Biomaterials*, **33**, 7164-7173. http://dx.doi.org/10.1016/j.biomaterials.2012.06.026

[45] Dhar, S., Gu, F.X., Langer, R., Farokhzade, O.C. and Lippard, S.J. (2008) Targeted Delivery of Cisplatin to Prostate Cancer Cells by Aptamer Functionalized Pt(IV) Prodrug-PLGA-PET Nanoparticles. *Proceedings of the National Academy of Sciences*, **105**, 17356-17361. http://dx.doi.org/10.1073/pnas.0809154105

[46] Yhee, J.Y., Koo, H., Lee, D.E., Choi, K. and Kwon, I.C. (2011). Multifunctional Chitosan Nanoparticles for Tumor Imaging and Therapy. *Advances in Polymer Science*, **243**, 139-161. http://dx.doi.org/10.1007/12_2011_119

[47] Du, H.L., Cai, X.Q. and Zhai, G.X. (2013) Advances in the Targeting Molecules Modified Chitosan-Based Nanoformu lations. *Current Drug Targets*, **14**, 1034-1052. http://dx.doi.org/10.2174/1389450111314090012

[48] Bergey, E.J., Levy, L., Wang, X.P., Krebs, L.J., Lal, M., Kim, K.S., Pakatchi, S., Liebow, C. and Prasad, P.N. (2002) DC Magnetic Field Induced Magnetocytolysis of Cancer Cells Targeted by LH-RH Magnetic Nanoparticles *in Vitro*. *Biomedical Microdevices*, **4**, 293-299. http://dx.doi.org/10.1023/A:1020906307053

[49] Nurunnabi, Md., Cho, K.J., Choi, J.S., Huh, Y.M. and Lee, Y.-K. (2010) Targeted Near-IR QDs-Loaded Micelles for Cancer Therapy and Imaging. *Biomaterials*, **31**, 5436-5444. http://dx.doi.org/10.1016/j.biomaterials.2010.03.057

[50] Xiao, Y.L., Hong, H., Javadi, A., Engle, J.W., Xu, W.J., Yang, Y.N., Zhang, Y. and Bamhart, T.E. (2012) Multifunctional Unimolecular Micelles for Cancer-Targeted Drug Delivery and Positron Emission Tomography Imaging. *Biomaterials*, **33**, 3071-3082. http://dx.doi.org/10.1016/j.biomaterials.2011.12.030

[51] Bailey, D.L., Townsend, D.W., Valk, P.E. and Maisey, M.N. (2005) Positron Emission Tomography: Basic Sciences. Springer-Verlag, Secaucus.

[52] Gubin, S.P. (2009) Magnetic Nanoparticles. Wiley-VCH, Weinheim. http://dx.doi.org/10.1002/9783527627561

[53] U.S. Food and Drug Administration (2014) Sunscreen.

[54] Mitchnick, M.A., Fairhurst, D. and Pinnell, S.R. (1999) Microfine Zinc Oxide (Z-Cote) as a Photostable UVA/UVB Sunblock Agent. *Journal of the American Academy of Dermatology*, **40**, 85-90. http://dx.doi.org/10.1016/S0190-9622(99)70532-3