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Review Article

Current status of nanotechnology in urology

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ABSTRACT

Nanotechnology has been investigated for its applications in medicine. The objective of this review was to summarize the current applications of nanotechnology in Urology. A systematic search of literature was performed and relevant articles were analyzed with specific reference to applications in Urology. Nanotechnology has applications in diagnostic urology like in uroimaging using nanoparticles and nanosensors. It has therapeutic applications in infections, malignancies, genetic disease using targeted drug delivery, gene transfers, nano device-based manipulations etc. Nanotechnology has many applications in Urology. More efforts are required to make these applications practically feasible and affordable.

Keywords: Nanotechnology, Urology, Nanoparticles, Nanomedicine

INTRODUCTION

Nanotechnology is a revolution that will have a tremendous bearing on the urological research and practice. Nanomedicine will help urologists better understand pathophysiology of diseases at molecular level. Almost every application of nanotechnology like nanosensors, nanoparticles, nanorobots and nanolasers etc. will have significant relevance to the diagnosis and treatment of urological conditions. The policy makers should ensure enough resources in terms of skilled manpower and infrastructure to carry on research in nanomedicine. Medical scientists and urologists should ensure to carry this knowledge from "laboratory to field". They should make every effort to provide the benefits of nanomedicine reach even lowest strata of society at affordable cost.

Nanotechnology is the technology on the scale of a billionth of a meter i.e. nanometer. To refer to increasingly precise machining and finishing of materials, progressing from larger to smaller scales and ultimately to nanoscale, N. Tanignchi first used the word 'Nanotechnology' in 1974.[1]

Nanomedicine is application of nanotechnology to the field of medicine. The first known use of term "Nanomedicne" was in 1991 by Drexler, Peterson and Pergamit in their popular book *"unbounding the future"*.[2] It refers to monitoring, repair, construction and control of human biological systems at the molecular level, using engineered nanodevices and nanostructure.[3] It was Freitas who first published nanomedical device design paper was in 1998 in the biotechnology journal "artificial cells".[4]

An electronic search to collect the data was performed using the PubMed/MEDLINE databases from January 2010 to March 2016. Using keywords "nanotechnology", "Urology" and "nanoparticles", 144 articles were found. Out of these 139 were full text articles. We also manually searched among the references of the identified articles. We restricted the search to articles published in English. All relevant articles were systematically analyzed with

specific reference to applications of nanotechnology in Urology.

DISCUSSION

Most of the disease processes start at cellular level. Functioning of these micron-sized cells is determined by nano-sized genes, proteins, enzymes and transmembrane nano-barriers. Thus for novel medicines to target specific locations within cells, passing through some biological barriers is a prerequisite. Conventional medicine, due to its micron-scale, does not have capability to be fully effective. Thus development of nanomedicine has made a significant progress in drug delivery in terms of ability to pass across nano-barriers and get access to molecules within cellular compartments. It has been proposed that almost all applications of nanotechnology have potential applications in biological systems.

Applications of nanotechnology in urology

The potential scope of nanotechnology in urology is wide-ranging. This ranges from prevention, early detection to drug delivery, symptom management and treatment of diseases. Nanotechnology also has applications in tissue engineering and gene therapy.

Diagnostic applications

The imaging techniques have progressed from simple X-rays and fluoroscopy to advanced techniques like computed tomography (CT), Magnetic resonance imaging (MRI), positron emission tomography (PET) etc. Despite these advancements, current uroimaging is limited in its efficacy a) in diagnosing malignancies in early stages, b) to detect micrometastasis, and c) to detect recurrence in curable stage following curative management. Nanomedicine has the potential to overcome many of these limitations. Nanoparticles have been widely explored for their applications in diagnostic urology. These include targeted imaging using nanoparticles like MNPs (magnetic nanoparticles), superparamagnetic nanoparticles and quantum dots etc. for detection of antigens, antibodies, receptors and single nucleotide polymorphisms etc.

Noninvasive imaging approaches such as computed tomography (CT), positron emission tomography (PET), Single photon emission computed tomography (SPECT) and magnetic resonance imaging (MRI) are used as important tools for detection of genitourinary cancers. These modalities using conventional contrast materials have limitations. As compared to conventional imaging, the use of nanoparticle based tumor-targeted agents has been shown to increase sensitivity and specificity of tumor imaging.[5] Magnetic nanoparticles (MNPs), by virtue of their nanosize, can extravasate into interstitial space and subsequently transported to lymphnodes where they are taken up by macrophages. This application can be used to detect metastasis to lymphnodes.[6] Within lymphnodes, lymphotropic superparamagnetic nanoparticles are internalized and change magnetic properties of tissue which are detectable by MRI.[7] Therefore lymphotropic nanotropic enhanced MRI **(**LNMRI**)** can be used to identify malignant nodal involvement in urological neoplasms with high sensitivity. Further "targeted LNMRI" will make this modality more specific in differentiating benign from malignant lymphnodes.

Prostate cancer is the most common malignancy of genitourinary system. After diagnosis of prostate cancer, accurate detection of lymphnode metastasis is essential to determine the extent of the disease to select appropriate treatment to the patient. As compared to conventional imaging, LNMRI had shown a significantly higher sensitivity of 90.5% (35.4% with conventional) for detection of malignant lymphnodes.[6] LNMRI have shown high sensitivity in accurate detection of lymphnode metastasis in renal and testicular malignancies.[8,9] Thus nanoparticle-based imaging will significantly improve the accuracy of metastasis detection in urological malignancies.

The diagnosis of genetic diseases using available modalities is still cumbersome, expensive and time-consuming. A rapid, accurate, and inexpensive nanoparticle-DNA based assay to detect polycystic kidney disease single nucleotide polymorphism mutations (PKD SNPs) have been developed.[10] By using only 0.02–0.05 ml of whole blood sample, this simple test can detect PKD SNPs with high sensitivity. This application of nanomedicine will make detection of genetic diseases (including carriers) early and easy. This will help in prevention and treatment of these diseases.

Infections constitute considerable bulk of urological diseases. With present modalities, sensitivity to identify culprit organisms in UTIs is low. Nanotechnology has been explored to diagnose urinary tract infections using nanosensors. Based on both optical and electrochemical nanoparticles and specific *E. coli* antibodies, a quick and sensitive procedure has been developed for bacterial detection in case of kidney infection.[11] The study showed that the biosensor can detect each of fifty *E. coli* cells with the sensor area of 0.178 cm^2. Nanosensor based microbial detection will not only improve diagnostic accuracy but also cure rates.

Therapeutic applications

Over the decades, attempts have been made to increase the efficacy and to reduce the morbidity and mortality of medical and surgical treatment of urological diseases. Nanomedicine appears to be promising in this regard. The nanocarrier-based targeted drug delivery and nanodevice-based molecular manipulation and tissue repair can help increase the efficacy of treatment while minimizing adverse-effects.

To investigate the efficacy of catheter associated UTI (CAUTI) prevention with the application of JUC (a nanotechnology antimicrobial spray), He et al conducted a multi-center clinical trial on 1150 patients. After 16 hours of culture, bacterial biofilm formed on the surface of sample fragments from the control group after 16 hours of culture. In the therapy group, no bacterial biofilm formation was found on the sample fragments. After 7 days of incubation, no significant increase in bacterial colony count was observed in the therapy group. Before extubation on the 7th day of catheterization, urine samples were collected for bacterial culture. Significant difference was observed in the incidence of bacteriuria between the therapy group and control group (4.52% versus 13.04%, $p<0.001$).[12]

Current chemotherapeutic drugs kill not only cancer cells, but also healthy cells. This not only causes significant toxicity to patients, but limits the dose and efficacy of the drug. The nanocarrier-based delivery of anticancer drugs to target tumor tissue can help to overcome this problem of chemotherapeutic drug treatment. Active targeting of tumor cells by conjugating the nanocarriers containing chemotherapeutics with molecules that bind to overexpressed antigens or receptors on the target cell will further help in increasing the efficacy and minimizing the drug toxicity.[13]

Treatment of prostate cancer, most common urological malignancy, is challenging. Efforts are on to improve the outcome and minimize the treatment related morbidity especially in metastatic and castrate-resistant prostate cancer. Nanoscale carrier molecules are being explored to achieve this objective. There are several examples of applications of chemotherapeutic drug loaded nanocarriers and targeted drug delivery for treating prostate cancer.

Doxorubicin has been the focus of investigation due to the fact that it is one of the most effective first-line anticancer therapeutics developed, but its toxicity in many organs limits its use.[13-16]

Doxil (doxorubicin), the first nanodrug approved by the USA Food and Drug Administration (FDA) in 1995, was based on the work by Barenholz on a liposomal-based doxorubicin formulation. A key concept in developing the doxorubicin-liposomes was the enhanced permeability and retention effect, which results from differences in vasculature between benign and malignant tissue. This allowed nanoparticles to cross and become selectively enriched in the tumor, with doxorubicin reaching 100-fold higher concentrations in the intraliposomal aqueous phase as compared with the loading medium.[14]

A significant improvement in the uptake of nanoparticles by PSMA (prostate specific membrane antigen) positive prostate cancer cells has been shown using nanoparticles conjugated with antibody against PSMA.[17,18] The over-expression of transferrin receptors on the surface of prostate cancer cells has been used to improve drug delivery in prostate cancer. In animal model, direct intratumoral injection of transferrin-conjugated paclitaxel-loaded nanoparticles showed complete tumor regression compared to paclitaxel-loaded nanoparticle without transferrin.[13]

A novel combi-molecule, JDF-12, with superior cytotoxicity against prostate cancer cells, was synthesized by Fang et al. But it has a poor stability in liquid after preparation with conventional method and is susceptible to hydrolysis and binding to organs highly expressing epidermal growth factor receptor (EGFR), resulting in side effects. Later, using biocompatible and biodegradable poly (D,L-lactic-co-glycolic acid)-block-poly (ethyleneglycol) (PLGA-b-PEG) copolymer and surface functionalized with a single-chain antibody, the JDF-12 loaded nanoparticles were formulated. This molecule recognizes the extracellular domain of prostate stem cell antigen (PSCA), enabling a controlled release, "stealth" property, and cell-specific targeting. The targeted nanoparticles were specifically endocytosed by prostate cancer cells though the receptor mediated endocytosis resulting in increased cellular toxicity in vitro. Moreover, a better outcome with reduced drug toxicity was observed in a PC3M xenograft animal model after treatment with these nanoparticles.[19]

In future, Nanoscale targeted carrier molecules can make the management of prostate cancer effective with little morbidity.

Cryotherapy and HIFU are already in use for management of prostate cancer. The possibility of use of nanocarriers for thermal therapy of prostate cancer is another interesting approach, particularly to treat the cancer which is refractory to chemotherapy. Thermal effect of magnetic nanoparticles has been explored in rat prostate cancer. It was found that when an alternating magnetic field (AMF) is applied to magnetic liposomes (MCLs), it generates heat and can increase the tumor temperature to 45°C. Significant tumor regression was observed in the animal model.[20] Similarly, near infrared (NIR) light has been used to generate heat instead of magnetic field. In vitro and in vivo study with ectopic murine prostate cancer model, laser activated gold nanoparticles have been shown to kill human prostate cancer cell.[21] These results will encourage the application of these noninvasive treatment modalities to human prostate cancer.

Intravesical chemotherapy, following transurethral tumor resection of superficial bladder cancer, has been used to reduce tumor recurrence and/or progression. However, the response of intravesical chemotherapy is incomplete and variable among patients; this is partly due to the inability of drug to penetrate bladder tissue. Nanocarriers loaded with chemotherapeutic drugs provide more efficient and specific approaches to treat bladder cancer

than free drug. The paclitaxel-loaded gelatin nanoparticles for intravesical chemotherapy has shown much higher drug concentrations in the urothelium and lamina propria than with Cremophor formulation.[22]

To further improve efficacy and to reduce side-effects, targeted intravesical chemotherapy has been explored. Bladder transitional cell carcinoma over-expresses the transferrin receptors on the surface of cells. The in vivo study showed that intravesical instillation of Tf-Lip–AlPcS4 (transferrin-conjugated liposomes aluminum phthalocyanine tetrasulfonate) resulted in accumulation of AlPcS4 (aluminum phthalocyanine tetrasulfonate) specifically in tumor cells whereas instillation of free AlPcS4 led to nonselective accumulation in bladder wall.[23] These results suggest that transferrin mediated liposomal targeting of photosensitizing drugs is a promising potential tool for photodynamic therapy of superficial bladder tumors.

Radical cystectomy is standard of care for muscle invasive bladder cancer. There are patients who are unfit for surgery or unwilling for radical surgery. Current modalities of treatment for such patients are not yielding encouraging results. Nanoparticle based targeted chemotherapy can improve outcome in this subset of patients. As compared to free drug, submucosal injection of doxorubicin loaded liposome in bladder was shown to result in better distribution of drug and prolonged retention through the bladder wall and regional lymphoid nodes.[24] Encouraging results in muscle invasive urothelial cancer can open the doors for bladder preservation in bladder cancer.

Han et al synthesized nanoparticles by putting tadalafil, sialorphin and NO into a topical gel. According to their study, nanoparticles encapsulating erectogenic agents were applied to the glans and penile shaft of rats. The control group consisted of nanoparticles, without the encapsulated erectogenic agent, applied to glans and penile shaft in a similar manner. Erectile response was seen within an average of 4.5 minutes after the administration of the topic agent comprised of NO nanoparticles, with a mean duration of 1.42 minutes. Sialorphin nanoparticles achieved a visible erectile response at an average time of 4.5 minutes after application and lasted for 8 minutes. Tadalafil nanoparticles were able to achieve an erectile response one hour after the stimulation of the cavernosal nerve.[25] This therapeutic application will be a boon for patients of erectile dysfunction as it will bypass systemic adverse effects.

Drug resistance is one of the major emerging obstacles limiting the therapeutic efficiency of chemotherapeutic or biologic agents. The mechanism of cancer drug resistance is complex and poorly understood. More often, it is due to the over-expression of multidrug drug resistance (MDR) transporters; the transporters actively pump chemotherapeutic drugs out of the cell and reduce the intracellular drug dose below lethal threshold levels. Nanocarriers can bypass the MDR by preventing anticancer drugs to encounter the transporters. Transferrin-conjugated (Tf-Tx-NPs) and unconjugated paclitaxel loaded nanoparticle (Tx-NPs) have shown cytotoxicity in drug resistant cell lines.[26] Thus Nanomedicine can help overcome imminent threat of drug resistance faced by medical scientists.

With the epidemic of diabetes mellitus and hypertension, number of patients suffering from end stage renal disease (ESRD) has increased several folds. The majority treatment of ESRD is intermittent haemodialysis and peritoneal dialysis. However, dialysis is associated with high mortality and morbidity with long-term use. Using nanotechnology, a renal replacement device named human nephron filter (HNF) has been developed. The HNF consist of two membranes, G membrane (mimics the function of the glomerulus) and T membrane (mimics the function of the renal tubules), operating in series within one cartridge. The HNF could provide the equivalent of 30 ml/min of glomerular filtration rate. The instrument is wearable and can permit full mobility.[27] When HNF will become practical reality, it will significantly improve the current outcomes and quality of life of ERSD patients.

Tissue engineering is an emerging field in medicine. It has been found that human bladder smooth muscle cells seeded on nano-surfaced scaffolds had shown increased cell adhesion, growth, and protein production compared with that seeded on the conventional, micro-dimensional scaffolds. The results suggested that nano-dimensional polymeric scaffolds could be promising replacement materials for human bladder wall in near future.[28] Applications of nanotechnology in regenerative medicine have begun to revolutionize stem cell research. It is hoped that ‘nano-based stem cell therapy’ will help recover renal function in end stage renal disease patients (ESRD).

Gene therapy, the transfer and expression of genes of therapeutic applications in the target cells, is regarded as a potential revolution in medicine.[29] The role of gene therapy lies in treatment of diseases at the genetic level. The carriers, which protect the ectopic genetic material and ferry it to the cells, are called ‘vectors’. Vectors are classified into two categories: viral and nonviral.

Viral vectors, though efficient cell-entry mechanism, have several major restrictions, such as limited DNA-carrying capacity, lack of target-cell specificity, immunogenicity and some viral vectors and the risk of insertional mutagenesis.[30] Nonviral vectors are relatively simple to synthesize and have fewer risks.

Current research in nanoparticles for gene therapy is focused mainly on liposomal models. This is because of their flexible construction, greater knowledge about their pharmacokinetic properties, and their effective ability to

carry nucleic acid and water insoluble drugs. However, cationic lipids alone are susceptible to nonspecific surface binding by serum proteins resulting in short circulation and fast clearance. Therefore, research is being carried out to design effective surface modifications for better nanoparticles gene carriers.[31-33]

Nanocarriers can be used as 'targeted nonviral vectors' which will overcome the limitations of viral vectors. Herpes simplex virus thymidine kinase (HSV-tk) gene delivered by folate-linked, lipid-based nanoparticles can achieve high transfection efficiency and selectivity, inhibiting tumor growth following intratumoral injection into prostate cancer.[34]

Research is going on improving QD (quantum dot) probe sensitivity and specificity in the detection of prostate cancer cells. Ma et al developed a novel carboxymethyl chitosan (CMC) coated CdTe QD. CMC possesses strong affinity for zinc and it induces an enhanced light signal when bound to the QD. Results showed a marked increase in sensitivity for detection of intracellular zinc. Likewise, the CMC coating on the QD surface reduced the potential toxicity of the QD nanoprobes.[35]

Surgical tools, such as 'nanotweezers' are under development, and it is expected that their use in microsurgical procedures such as vasectomy reversal and varicocele repair will bw reality in near future. In addition, nanoprobes aiding diagnostic procedures, e.g. 'nano-urobots' that could be used for cystoscopy, ureteroscopy and fulguration of tumours, as well as searching the venous involvement by renal cell cancer, may be imminent. 'Smart' nanosensors with communication capability are being developed, with particular interest in urological tissue engineering for urinary tract reconstruction.[3]

Nanolaser, a latest application of nanotechnology, is a laser that has nanoscale dimensions. The nanolaser concept was developed by Mark Stockman at Georgia State University in 2003. These tiny lasers can be modulated quickly and, combined with their small footprint, this makes them ideal candidates for on-chip optical computing. The intense optical fields of such a laser also enable the enhancement effect in non-linear optics or surface-enhanced-raman-scattering.[36-38] Nanolasers, once practically viable, may have role in excising diseased tissues at nanoscale e.g. nanometastasis.

Limitations of nanotechnology

As with all new technologies, there are potential problems associated with nanomedicine in urology. Ethical, socioeconomic, political and environmental concerns will have to be fully addressed before it becomes standard practice. Clearly, there will a requirement for stringent national and international rules and regulations to prevent potential misuse, such as "genetic colonialism" and for terrorist activities.

Future of nanotechnology

The future of nanomedicine was highlighted in a report by a panel of U.S. Department of Defense health science experts on Nanomedicine in 1997 as[39]: "If a breakthrough to a [molecular] assembler occurs within ten to fifteen years, an entirely new field of nanomedicine will emerge by 2020. Initial applications will be focused outside the body in areas such as diagnostics and pharmaceutical manufacturing. The most powerful uses would eventually be within the body.

Possible applications include programmable immune machines that travel through the bloodstream, supplementing the natural immune system; cell herding machines to stimulate rapid healing and tissue reconstruction; and cell repair machines to perform genetic surgery".

Nanosystems which were fictional have become reality. These have found their applications in diagnostic and therapeutic urology. The future of nanomedicine lies in preventive and regenerative medicine. The applications of nanotechnology are being explored to regenerate tissues and organs which are terminally damaged. In future, nanotechnology based drugs and devices etc. will help diagnose and cure the genetic diseases and congenital anomalies at prenantal level.

The full capabilities of these nanomachines will not be realized without a great deal of sweat and toil by legions of well-funded and dedicated researchers working for many decades to develop the technology and bring that technology from laboratory to field.

CONCLUSION

Nanotechnology is a revolution that will have a tremendous bearing on the urological research and practice. Nanomedicine will help urologists better understand pathophysiology of diseases at molecular level. Almost every application of nanotechnology like nanosensors, nanoparticles, nanorobots and nanolasers etc. will have significant relevance to the diagnosis and treatment of urological conditions. The policy makers should ensure enough resources in terms of skilled manpower and infrastructure to carry on research in nanomedicine. Medical scientists and urologists should ensure to carry this knowledge from "laboratory to field". They should make every effort to provide the benefits of nanomedicine reach even lowest strata of society at affordable cost.

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REFERENCES

1. Taniguchi N. On the basic concept of 'nano-technology'. Proc Intl Conf Prod Eng Tokyo, Part II, Japan Society of Precision Engineering, 5–10.
2. Drexler KE. Unbounding the future: The nanotechnology revolution. New York: Harper Collins; 1991.
3. Shergill IS, Rao A, Arya M, Patel H, Gill IS. Nanotechnology: Potential applications in Urology. BJU International. 2006;97:219-25.
4. Freitas RA Jr. Exploratory design in medical Nanotechnology: A Mechanical Artificial Red Cell, Artificial Cells, Blood Substitutes, and Immobil. Biotech. 1998;26:411-30.
5. Sun C, Lee JS, Zhang M. Magnetic nanoparticles in MR imaging and drug delivery. Adv Drug Del Rev. 2008;60(11):1252-65.
6. Harisinghani MG, Barentsz J, Hahn PF. Noninvasive detection of clinically occult lymph-node metastases in prostate cancer. New Engl J Med. 2003;348(25):2491-9.
7. Wunderbaldinger P, Josephson L, Bremer C, Moore A, Weissleder R. Detection of lymph node metastases by contrast-enhanced MRI in an experimental model. Magn Reson Med. 2002;47(2):292-7.
8. Guimaraes AR, Tabatabei S, Dahl D, McDougal WS, Weissleder R, Harisinghani MG. Pilot study evaluating use of lymphotrophic nanoparticle-enhanced magnetic resonance imaging for assessing lymph nodes in renal cell cancer. Urology. 2008;71(4):708-12.
9. Harisinghani MG, Saksena M, Ross RW, Tabatabaei S, Dahl D, McDougal S, et al. A pilot study of lymphotrophic nanoparticle-enhanced magnetic resonance imaging technique in early stage testicular cancer: a new method for noninvasive lymph node evaluation. Urology. 2005;66(5):1066-71.
10. Son A, Dhirapong A, Dosev DK, Kennedy IM, Weiss RH, Hristova KR. Rapid and quantitative DNA analysis of genetic mutations for polycystic kidney disease (PKD) using magnetic/luminescent nanoparticles. Anal Bioanal Chem. 2008;390(7):1829-35.
11. Basu M, Seggerson S, Henshaw J, Jiang J, del A Cordona R, Lefave C, et al. Nano-biosensor development for bacterial detection during human kidney infection: use of glycoconjugate-specific antibody-bound gold NanoWire arrays (GNWA). Glycoconj J. 2004;21(8-9):487-96.
12. Wei He W, Wang D, Ye Z, Qian W, Tao Y, Shi X, et al. Application of a nanotechnology antimicrobial spray to prevent lower urinary tract infection: a multicenter urology trial. Journal of Translational Medicine. 2012;10(Suppl 1):S14.
13. Sahoo SK, Ma W, Labhasetwar V. Efficacy of transferrin-conjugated paclitaxel-loaded nanoparticles in a murine model of prostate cancer. Int J Cancer. 2004;112(2):335-40.
14. Barenholz Y. Doxil® – the first FDA approved nano-drug: lessons learned. J Control Release. 2012;160:117-34.
15. McNealy TL, Trojan L, Knoll T, Alken P, Michel MS. Micelle delivery of doxorubicin increases cytotoxicity to prostate carcinoma cells. Urol Res. 2004;32(4):255-60.
16. Thangapazham RL, Puri A, Tele S, Blumenthal R, Maheshwari RK. Evaluation of a nanotechnology based carrier for delivery of curcumin in prostate cancer cells. Int J Oncol. 2008;32(5):1119-23.
17. Cheng J, Teply BA, Sherifi I, Sung J, Luther G, Gu FX, et al. Formulation of functionalized PLGA-PEG nanoparticles for in vivo targeted drug delivery. Biomaterials. 2007;28(5):869-76.
18. Patri AK, Myc A, Beals J, Thomas TP, Bander NH, Baker JR Jr. Synthesis and in vitro testing of J591 antibody-dendrimer conjugates for targeted prostate cancer therapy. Bioconjug Chem. 2004;15 (6):1174-81.
19. Fang Y, Wu J, Li T, Liu W, Gao L, Luo Y. Nanoparticle mediated chemotherapy of hormone refractory prostate cancer with a novel combi-molecule. Am J Transl Res. 2015;7(8):1440-9.
20. Kawai N, Futakuchi M, Yoshida T, Ito A, Sato S, Naiki T, et al. Effect of heat therapy using magnetic nanoparticles conjugated with cationic liposomes on prostate tumor in bone. Prostate. 2008;68(7):784-92.
21. Stern JM, Stanfield J, Kabbani W, Hsieh JT, Cadeddu JA. Selective prostate cancer thermal ablation with laser activated gold nanoshells. J Urol. 2008;179(2):748-53.
22. Lu Z, Yeh TK, Tsai M, Au JL, Wientjes MG. Paclitaxel-loaded gelatin nanoparticles for intravesical bladder cancer therapy. Clin Cancer Res. 2004;10(22):7677-84.
23. Derycke AS, Kamuhabwa A, Gijsens A, Roskams T, De Vos D, Kasran A, et al. Transferrin-conjugated liposome targeting of photosensitizer AlPcS4 to rat bladder carcinoma cells. J Natl Cancer Inst. 2004;96(21):1620-30.
24. Kiyokawa H, Igawa Y, Muraishi O, Katsuyama Y, Iizuka K, Nishizawa O. Distribution of doxorubicin in the bladder wall and regional lymph nodes after bladder submucosal injection of liposomal doxorubicin in the dog. J Urol. 1999;161(2):665-7.
25. Peer D, Karp JM, Hong S, Farokhzad OC, Margalit R, Langer R. Nanocarriers as an emerging platform for cancer therapy. Nat Nanotechnol. 2007;2(12):751-60.
26. Sahoo SK, Labhasetwar V. Enhanced antiproliferative activity of transferrin-conjugated paclitaxel loaded nanoparticles is mediated via sustained intracellular drug retention. Mol Pharm. 2005;2(5):373-83.
27. Nissenson AR, Ronco C, Pergamit G, Edelstein M, Watts R. Continuously functioning artificial

nephron system: the promise of nanotechnology. Hemodial Int. 2005;9(3):210-7.
28. Pattison MA, Wurster S, Webster TJ, Haberstroh KM. Three-dimensional, nano-structured PLGA scaffolds for bladder tissue replacement applications. Biomaterials. 2005;26(15):2491-2500.
29. Verma IM, Somia N. Gene therapy -- promises, problems and prospects. Nature. 1997;389(6648):239-42.
30. Mastrobattista E, van der Aa MA, Hennink WE, Crommelin DJ. Artificial viruses: a nanotechnological approach to gene delivery. Nat Rev Drug Discov. 2006;5(2):115-21.
31. Tyagi P, Wu PC, Chancellor M, Yoshimura N, Huang L. Recenadvances in intravesical drug/gene delivery. Mol Pharm. 2006;3:369-79.
32. Hadinoto K, Sundaresan A, Cheow WS. Lipid-polymer hybrid nanoparticles as new generation therapeutic delivery platform: a review. Eur J Pharm Biopharm. 2013;85:427-43.
33. Fortier C, Durocher Y, De Crescenzo G. Surface modification of nonviral nanocarriers for enhanced gene delivery. Nanomedicine (Lond). 2014;9:135-51.
34. Hattori Y, Maitani Y. Folate-linked lipid-based nanoparticle for targeted gene delivery. Curr Drug Del. 2005;2(3):243-52.
35. Ma Q, Lin ZH, Yang N, Li Y, Su XG. A novel carboxymethyl chitosan-quantum dot-based intracellular probe for ZN(2+) ion sensing in prostate cancer cells. Acta Biomater. 2014;10: 868-74.
36. Anker, Jeffrey N. Biosensing with plasmonic nanosensors. Nature Materials. 2008;7:442-53.
37. Oulton RF. Plasmon lasers at deep subwavelength scale. Nature. 2009;461:629-32.
38. Khajavikhan M. Thresholdless nanoscale coaxial lasers. Nature. 2012;482:204-7.
39. Olson R. Focused Study on Biotechnology and Nanotechnology, Military Health Service System (MHSS)-2020, U.S. Department of Defense, Health Affairs, September.

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