

Various Nanotechnology platforms in cancer prevention, detection and treatment- A Review

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Abstract: A Cancer is a disease in which abnormal cells divide uncontrollably and destroys body tissue. It is caused by damage of genes which control the growth and division of cells. In the fight against cancer, early detection is a key factor for successful treatment. However, the detection of cancer in the early stage has been hindered by the intrinsic limits of conventional cancer diagnostic methods. Nanotechnology provides high sensitivity, specificity, and multiplexed measurement capacity and has therefore been investigated for the detection of extracellular cancer biomarkers and cancer cells, as well as for in vivo imaging. These advances will improve the survival rate of cancer patients by enabling early detection. In addition, it could be used to monitor cancer progress in response to treatment, which may contribute to the development of better strategies for cancer treatment. This review paper is an overview of various nanotechnology platforms in cancer prevention, detection and treatment.

Keywords: Nanotechnology, Nanoparticles, Cancer diagnosis, Cancer biomarker.

1. INTRODUCTION

A Cancer is a disease in which abnormal cells divide uncontrollably which destroys body tissue and spread to other parts of the body. The normal cells are transformed into cancerous cells when genetic factors of a person interact with some external agents like physical, chemical and biological carcinogens which are a multistage process. It remains as one of the most common cause of death [1,18]. Generally 90-95% cases on cancer are induced by environmental factors. The remaining 5-10% is due to inherited genetics. There are about 100 different cancer types out of which the common ones are lung, stomach, liver, oesophagus, colorectal, breast, melanoma and cervical cancer. The conventional methods which are still in practice include surgery, chemotherapy, radio therapy and targeted therapy. Surgery and radio therapy allows the removal of cancer cells only to that specific targeted area and chemotherapy that allows the drug to flow through the bloodstream or can be delivered directly to the specific area. Targeted therapy is a newer technique that allows the removal of cancer cells more precisely and thus leading to less damage to normal cells. The effectiveness of treatment can be judged on the basis of drug's ability to target and kill cancer cells while leaving healthy cells intact. The most important feature should be differentiation of healthy and affected cells. Another factor to be taken into consideration is the biocompatibility of the drug such that the side effects are reduced. The current available techniques are lacking behind when it comes the aforementioned factors. Newer techniques like nanotechnology are currently in research since it provides a promising approach when it comes to cancer cell selectivity and reduced side effects.

Nanotechnology is a science which deals with processes that occur at molecular end; supra molecular level resulting in nanoparticles of unique properties such as increased solubility and bio compatibility. It has wide ranging applications such as bio-sensors [2,3,27]. Due to increased surface modification properties, it can be used in targeted delivery in case of cancer detection. Nano-systems have an edge over conventional methods when it comes to drug delivery and toxicity. Some of the nanoparticles used for cancer detection and treatment include liposomes, dendrimers, fullerene, quantum dots, magnetic nanoparticles, gold nanoparticles, nano-wires, nanoshells and carbon-nanotubes. Nanotechnology in conjunction with medicine provides an important platform where nano-carriers can be manipulated as well as used for multifunctional properties. It is one of the most promising approaches in detection and treatment of cancer.

2. BACKGROUND

The nanoparticles must have high loading capacity for selected drug, high response to stimuli, high bioavailability and stability. In addition to this, specific targeting, long circulation and intracellular delivery are some of the features. Nano-systems can identify biomarkers and detect tumor cells. In this line, nanotechnology protects drug from degradation before they reach their target and enhances absorption of drugs into tumors. Another conclusion we can draw is that using nanoparticles, the drug release rates can be precisely controlled while reducing the side-effects. The

nanoparticles which are used as drug delivery vehicles are generally <100 nm in size and they consist of different biodegradable materials such as natural or synthetic polymers, metals or lipids along with their applications [5, 7, 9, 11]. Two of the nanoformulated drugs available in the market today are Abraxine and Doxil. Abraxine is a human albumin based nano-formulated drug with a size of around 100nm. It is also known as ABI-007 or nanoparticle albumin bound [nab]-Paclitaxel [PTX]. To reduce side effects, albumin has been used to conjugate PTX with Cremophor. Doxil is the formulation of doxorubicin in nano-liposome and has shown significant improvements over free doxorubicin. In some other clinical trials, various combinations of drugs have been implemented.

3. PLATFORMS FOR CANCER THERAPY

The most common nanotechnology platforms for cancer therapy include polymeric nanoparticles, Quantum dots, carbon nanotubes, Metallic nanoparticles, liposomes, dendrimers, nanoshells, and superparamagnetic nanoparticles[35,79]. With small size and various structural and physicochemical features, these nanotechnology platforms can enter tumor vasculature through enhanced permeability and retention effect (EPR). The use of cancer-specific targeting residues (e.g. antibodies, ligands, and lectins) can also achieve tumor cell targeting.

3.1 Polymeric nanoparticles

The preparation of Polymeric nanoparticles are done from natural or synthesized polymers. Various biodegradable or unbiodegradable polymers can be used to prepare nanoparticles in order to achieve expected drug delivery performance and therapeutic effect[65,69]. Among these, biodegradable polymeric nanoparticles for anticancer drug delivery have attracted great interest in recent years since they could provide controlled, sustained and targeted delivery. Polymeric nanoparticles, the most effective nanotechnology platforms, have emerged as a versatile carrier system for targeted delivery of anticancer drugs.

3.2 Quantum dots

The Quantum dots are nano-crystals ranging from 2-10nm which have extensively attracted great interest in the field of biology and medicine because of its unique optical and electrical properties. They have a distinct advantage over conventional biomarkers because of their high photo stability and size tunable excitation[42,49]. Use of quantum dots has been extended in the NIR wavelength range as an imaging probe. The main advantage of the technique is that it increases the depth of tissue penetration which will lead to more accurate detection in-vivo. Materials best suited in building up quantum dots are cadmium sulphide and cadmium selenide. However, based on factors like toxicity and bio-compatibility, Zinc Sulfide is preferred. Applications of quantum dots include in-vivo and in-vitro imaging, live cell imaging and single molecule tracking[52,58]. It is used for the detection of lung cancer, breast cancer, prostate cancer and pancreatic cancer, detection of primary tumor in vitro, prostate cancer, targeting and imaging melanoma and also detection of thyroid carcinoma antigen.

3.3 Carbon Nanotubes

The Carbon Nanotubes belong to the family of fullerenes and are formed of coaxial graphite sheets (<100 nm) rolled up into cylinders. Structurally there are two types: single-walled carbon nanotubes (SWCNTs) and multi-walled carbon nanotubes (MWCNTs). It possesses properties such as high aspect ratio, ultralight weight, tremendous strength and high thermal conductivity. In the field of cancer, diagnostic and therapeutic, three main properties have been exploited i.e., small size, high surface area to volume ratio and their ability to contain chemicals[66,69]. Surface of carbon nanotubes can be modified with proteins for cellular uptake which are then heated up upon absorbing near-IR light wave. When exposed to near-IR light, carbon nanotubes quickly release excess energy as heat (~70°C) which can kill cancerous cells. Due to their unique properties, they have wide ranging applications in cancer diagnosis and therapy. Some of the notable applications in cancer diagnosis are molecular imaging with single-walled carbon nanotubes and cancer biomarker detection. It is also used for drug delivery and thermal therapy. The CNTs have proposed as a promising tool for detecting cancer at early stages with high sensitivity, selectivity and low detection limit.

3.4 Metallic nanoparticles

They have attractive properties like high surface Plasmon resonance, optical properties which can be tuned from visible to infra-red range. They possess large surface energy and have the ability to absorb small molecules. Gold, silver and platinum are some of the metallic nanoparticles that have been used for cancer diagnosis and therapy[33,38]. The Gold nanoparticles have already been used as a vehicle for the delivery of anti-cancer drugs such as paclitaxel. Properties of gold nanoparticles including small size, bio-compatibility, high atomic number and ability to bind targeting agents gives an advantage over other nanoparticles to be used as contrast agents. The formation of bubble around the overheated gold nanoparticles in liquid environment followed by generation of acoustic and shock waves protein inactivation has become a profound area of research. The Gold has also been used together with magnetic materials to improve the

photo thermal effect to accelerate the death of cancer cells. The Limitations like toxicity and larger nanoparticles involves in targeting of silver nanoparticles to cancer cells.

3.5 Liposomes

They are small artificial vesicles which are incredibly biodegradable. Confinement and protection of the drug enclosed is done by the fatty layer on the liposomes. In this process, efficacy is improved keeping toxicity to healthy cells minimized [51,59]. Their size ranges from 25nm to 10 μ m depending on the preparation method. Sizes which are less than 400nm can rapidly penetrate tumour sites from the blood stream by the endothelial wall in healthy tissue vasculature. Because of their unique structure, liposomes are considered as a versatile platform for combination drug delivery because they can simultaneously load hydrophilic drugs in their aqueous core and hydrophobic drugs in their lipid bilayered membrane. Some of the liposomal products used currently for cancer treatment include Doxil, DaunoXome®, DepoCyt® and ONCO-TCS, which are liposomal formulations of doxorubicin, daunorubicin, cytarabine and vincristine, respectively.

3.6 Dendrimers

Generally Dendrimers possess multiple branches which is advantageous when it comes to multifunctional applications. In cancer, treatment and drug delivery systems can be used to carry multiple drugs at the same time to tumor site improving efficiency and reduces the time constraint. It has gained interest because of their cylindrical structures which often comes with unique properties [29,38]. Sensitivity of imaging can be improved since they can be targeted to a single site and the unique architecture enables for multivalent attachment of imaging probes, as well as targeting moieties. In this way, it improves the therapeutic index of cytotoxic drugs by direct delivery to cancer cells and also offers drug resistance in tumor cells.

3.7 Nanoshells

Nanoshells are type of other nanoparticles which are being lined up in cancer therapeutics and diagnostics. They are composed of a gold shell surrounding a semiconductor. When they reach the cancer cells, they can be irradiated. These irradiations make them hot which ultimately kill the cancer cells. This technique has been successfully utilized in veneral tumours in mice.

3.8 Magnetic nanoparticles

The Magnetic nanoparticles have been used in biomedical field including cancer treatment. One of the most widely used nanoparticle of this kind are the Super magnetic iron oxide nanoparticles (SPIONs). One of the distinguishing features of SPIONs for drug deliver is their applicability for both magnetic properties and anti-body attachment which will improve targeting capability [71,76]. Magnetic iron oxide particles offer a huge advantage over the other particles since they are highly bio-compatible. Magnetic nanoparticles are currently in development as a promising new type of cancer treatment which selectively heat tumor cells to temperatures high enough to kill cancer cells without harming normal ones. This destroys tumors and leads to the activation of immune system to attack other cells throughout the body. In this process, the heat produced can kill the cancer cells and releases the drug from the nanoparticles directly inside the cancer cells. Magnetic radiated hyperthermia can be used for local tumor treatments.

4. ADVANTAGES AND CHALLENGES OF NANOTECHNOLOGY FOR CANCER THERAPY

The Nanotechnology has got many advantages in cancer therapy. With small size, nanotechnology platforms can enter tumor vasculature via EPR. Besides, functionalization with hydrophilic polymer/oligomer can offer a long circulation half-life and prolong the exposure time of tumor tissue to anticancer agents; Whereas inclusion of tissue-recognition residues, such as antibodies, lectins and ligands which are specific for cancer cells, can help nanotechnology platforms achieve tumor cell targeting. For overcoming MDR of cancer cells, a major challenge in effective cancer therapy, combinations of multi-functional nanotechnology platforms and other therapies have been developed and achieved significant successes [71,73].

However, there are still challenges to the development and application of nanotechnology platforms in cancer therapy, such as limited knowledge of the cancer cell physiology, small variety and poor functionalization of medical nanomaterials, and deficiency of clinical evaluation criteria. Nonetheless, with further advances in functionalization base on thorough understanding of the physiological features of cancer cells, nanotechnology platforms hold the promise of essentially changing the practice of oncology, allowing easy and effective targeted therapies.

5. CONCLUSION

Several methods and protocols such as chemotherapy, radiology and surgery have been used which has many side effects that make patients feel unbearable pain and deep anxiety. The emergence of nanotechnology has made a significant effect on cancer detection and treatment. Nanotechnology has the ability to serve as a tool which can change the foundation of cancer diagnostic treatment and prevention. The main advantage is the small size of nanoparticles which helps in reaching the roots of cancer cells. Advanced and effective drug delivery systems have been designed in the past few years. Some of the nanoparticles used in Cancer therapy have unique properties like bio-compatibility which becomes ideal when designing effective systems. Nano-systems can not only cure cancer but can also cure damage cells and regeneration of cells. The use of nanoparticles can improve the harmful side effects of conventional techniques like chemotherapy and radiotherapy. Deposition of the selective heat to tumor cells is another advantage of nanotechnology which provides a versatile platform to cure cancer. Different types of cancer cells have unique properties that can be exploited by nanoparticles to target the cancer cells. In future, nano-robots could repair disease cells, eliminate bacterial infection in a patient without using treatment with antibiotics, perform surgery at the cellular level, remove individual disease cell and even repair the defective portion of defective cell. Nanotechnology has greater potential to save lives than any other method that we use today. It has become a boon in medical field even by delivering drugs to specific cells using nanoparticles. Cancer nanotechnology definitely can provide a breakthrough to eradicate cancer related death.

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REFERENCES

1. The, L., LANCET, (2018) 392, 985. [PubMed]
2. Howlader N, Noone AM, Krapcho M, Garshell J, Neyman N, Altekruse SF, Cronin KA, Howlander N, Aminou R, Waldron. W. 2015.
3. Rezaianzadeh A, Jalali M, Maghsoudi A, Mokhtari AM, Azgomi SH, Dehghani SL. Breast Dis. 2017;**37**:1. [Google Scholar]
4. Listed N. Dukemed Healthnews. 2010;**16**:8. [Google Scholar]
5. Choi YE, Kwak JW, Park JW. Sensors (Basel) 2010;**10**:428. doi: 10.3390/s100100428. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
6. Chinen AB, Guan CM, Ferrer JR, Barnaby SN, Merkel TJ, Mirkin CA. Chem Rev. 2015;**115**:10530. doi: 10.1021/acs.chemrev.5b00321. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
7. Zhou W, Gao X, Liu D, Chen X. Chem Rev. 2015;**115**:10575. doi: 10.1021/acs.chemrev.5b00100. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
8. Song S, Qin Y, He Y, Huang Q, Fan C, Chen HY. Chem Soc Rev. 2010;**39**:4234. doi: .1039/c000682n. [PubMed] [CrossRef] [Google Scholar]
9. Chen XJ, Zhang XQ, Liu Q, Zhang J, Zhou G. J Nanobiotechnol. 2018;**16**:52. doi: 10.1186/s12951-018-0378-6. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
10. Chevillet JR, Lee I, Briggs HA, He Y, Wang K. Molecules. 2014;**19**:6080. doi: 10.3390/molecules19056080. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
11. Borrebaeck CA. Nat Rev Cancer. 2017;**17**:199. doi: 10.1038/nrc.2016.153. [PubMed] [CrossRef] [Google Scholar]
12. Ueda K. Proteomics Clin Appl. 2013;**7**:607. [PubMed] [Google Scholar]
13. Ma, H.; Liu, J.; Ali, M. M.; Mahmood, M. A.; Labanieh, L.; Lu, M.; Iqbal, S. M.; Zhang, Q.; Zhao, W.; Wan, Y., Chem Soc Rev, (2015) 44, 1240. [PubMed]
14. Ponomaryova A, Rykova E, Cherdynseva N, Morozkin E, Zaporozhchenko I, Skvortsova T, Dobrodeev A, Zav Yalov A, Tuzikov S, Vlassov V. Ejc Supplements. 2015;**13**:43. doi: 10.1016/j.ejcsup.2015.08.077. [CrossRef] [Google Scholar]
15. Hull LC, Farrell D, Grodzinski P. Biotechnol Adv. 2014;**32**:666. doi: 10.1016/j.biotechadv.2013.08.003. [PubMed] [CrossRef] [Google Scholar]
16. Sharifi M, Avadi MR, Attar F, Dashtestani F, Ghorchian H, Rezayat SM, Saboury AA, Falahati M. Biosens Bioelectron. 2018;**126**:773. doi: 10.1016/j.bios.2018.11.026. [PubMed] [CrossRef] [Google Scholar]
17. Doria Gonçalo, Conde João, Veigas Bruno, Giestas Leticia, Almeida Carina, Assunção Maria, Rosa João, Baptista Pedro V. Noble Metal Nanoparticles for Biosensing Applications. Sensors. 2012;**12**(2):1657–1687. doi: 10.3390/s120201657. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

18. Harun Noor Aniza, Benning Matthew J., Horrocks Benjamin R., Fulton David A. Gold nanoparticle-enhanced luminescence of silicon quantum dots co-encapsulated in polymer nanoparticles. *Nanoscale*. 2013;5(9):3817. doi: 10.1039/c3nr00421j. [PubMed] [CrossRef] [Google Scholar]
19. Wu, T. L.; Sun, Y. C.; Chang, P. Y.; Tsao, K. C.; Sun, C. F.; Wu, J. T., *J CLIN LAB ANAL*, (2010) 17, -. [PMC free article] [PubMed]
20. Medintz, I. L.; Uyeda, H. T.; Goldman, E. R.; Mattoussi, H., *NAT MATER*, (2005) 4, 435. [PubMed]
21. Freeman, R.; Willner, I., *CHEM SOC REV*, (2012) 41, 4067. [PubMed]
22. Li, H.; Cao, Z.; Zhang, Y.; Lau, C.; Lu, J., *ANALYST*, (2011) 136, 1399. [PubMed]
23. Gu, B.; Xu, C.; Yang, C.; Liu, S.; Wang, M., *BIOSENS BIOELECTRON*, (2011) 26, 2720. [PubMed]
24. Wang J, Jiang S, Li Z, Diflorioalexander RM, Barth RJ, Kaufman PA, Pogue BW, Paulsen KD. *MED PHYS*. 2010;37:3715. doi: 10.1118/1.3455702. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
25. Yun, W.; Zhang, X.; Xiong, Z.; Zhen, C.; Fisher, D. R.; Shuang, L.; Gambhir, S. S.; Chen, X., *Journal of Nuclear Medicine Official Publication Society of Nuclear Medicine*, (2005) 46, 1707.
26. Puigsauss, C.; Rojas, L. A.; Laborda, E.; Figueras, A.; Alba, R.; Fillat, C.; Alemany, R., *GENE THER*, (2014) 21, 767. [PubMed]
27. Jin, J.; Xu, Z.; Zhang, Y.; Gu, Y. J.; Lam, M. H.; Wong, W. T., *ADV HEALTHC MATER*, (2013) 2, 1501. [PubMed]
28. Mehra, R.; Tomlins, S. A.; Yu, J.; Cao, X.; Wang, L.; Menon, A.; Rubin, M. A.; Pienta, K. J.; Shah, R. B.; Chinnaiyan, A. M., *CANCER RES*, (2008) 68, 3584. [PMC free article] [PubMed]
29. Tong R, Coyle VJ, Tang L, Barger AM, Fan TM, Cheng J. *Microsc Res Tech*. 2010;73:901. doi: 10.1002/jemt.20824. [PubMed] [CrossRef] [Google Scholar]
30. Sharipov M, Tawfik SM, Gerelkhuu Z, Huy BT, Lee YI. *Sci Rep*. 2017;7:16073. doi: 10.1038/s41598-017-16136-4. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
31. Schwaederlé Maria C., Patel Sandip P., Husain Hatim, Ikeda Megumi, Lanman Richard B., Banks Kimberly C., Talasaz AmirAli, Bazhenova Lyudmila, Kurzrock Razelle. Utility of Genomic Assessment of Blood-Derived Circulating Tumor DNA (ctDNA) in Patients with Advanced Lung Adenocarcinoma. *Clinical Cancer Research*. 2017;23(17):5101–5111. doi: 10.1158/1078-0432.CCR-16-2497. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
32. Sohrabi, N.; Valizadeh, A.; Farkhani, S. M.; Akbarzadeh, A., *Artif Cells Nanomed Biotechnol*, (2016) 44, 654. [PubMed]
33. Tan SJ, Yeo T, Sukhatme SA, Kong SL, Lim WT, Lim CT. Personalized Treatment Through Detection and Monitoring of Genetic Aberrations in Single Circulating Tumor Cells. 2017. [PubMed] [Google Scholar]
34. Borghei YS, Hosseini M, Ganjali MR. *Methods Appl Fluoresc*. 2017;6:15001. doi: 10.1088/2050-6120/aa8988. [PubMed] [CrossRef] [Google Scholar]
35. Jou AF, Lu CH, Ou YC, Wang SS, Hsu SL, Willner I, Ho JA. *CHEM SCI*. 2015;6:659. doi: 10.1039/C4SC02104E. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
36. Sina AA, Carrascosa LG, Liang Z, Grewal YS, Wardiana A, Shiddiky M, Gardiner RA, Samaratunga H, Gandhi MK, Scott RJ, Korbie D, Trau M. *NAT COMMUN*. 2018;9:4915. doi: 10.1038/s41467-018-07214-w. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
37. Ko J, Bhagwat N, Black T, Yee SS, Na YJ, Fisher SA, Kim J, Carpenter EL, Stanger BZ, Issadore D. *CANCER RES*. 2018:2017.
38. Jiang Y, Shi M, Liu Y, Wan S, Cui C, Zhang L, Tan W. *Angewandte Chemie*. 2017;56:11916. doi: 10.1002/anie.201703807. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
39. Gupta GP, Massague J. *CELL*. 2006;127:679. doi: 10.1016/j.cell.2006.11.001. [PubMed] [CrossRef] [Google Scholar]
40. Chaffer CL, Weinberg RA. *SCIENCE*. 2011;331:1559. doi: 10.1126/science.1203543. [PubMed] [CrossRef] [Google Scholar]
41. Hong, W.; Lee, S.; Chang, H. J.; Lee, E. S.; Cho, Y., *BIOMATERIALS*, (2016) 106, 78. [PubMed]
42. Wen, C. Y.; Wu, L. L.; Zhang, Z. L.; Liu, Y. L.; Pang, D., *ACS NANO*, (2013) 8, [PubMed]
43. Wu Chun-Hsien, Huang Yu-Yen, Chen Peng, Hoshino Kazunori, Liu Huaying, Frenkel Eugene P., Zhang John X. J., Sokolov Konstantin V. Versatile Immunomagnetic Nanocarrier Platform for Capturing Cancer Cells. *ACS Nano*. 2013;7(10):8816–8823. doi: 10.1021/nn403281e. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
44. Pang X, Cui C, Su M, Wang Y, Wei Q, Tan W. *NANO ENERGY*. 2018;46:101. doi: 10.1016/j.nanoen.2018.01.018. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
45. Changfeng, W.; Thomas, S.; Maxwell, Z.; Jiangbo, Y.; Schiro, P. G.; Burnham, D. R.; McNeill, J. D.; Chiu, D. T., *J AM CHEM SOC*, (2010) 132, 15410.
46. Zhu, Y.; Chandra, P.; Shim, Y., *ANAL CHEM*, 85, 1058. [PubMed]
47. Zhang, Y.; Chen, B.; He, M.; Yang, B.; Zhang, J.; Hu, B., *ANAL CHEM*, 86, 8082. [PubMed]

48. Huang, Q.; Fu-Bing, W.; Chun-Hui, Y.; Zhaobo, H.; Lang, R.; Bo, C.; Bolei, C.; Susu, J.; Zhiqiang, L.; Jincao, C., THERANOSTICS, 8, 1624. [PMC free article] [PubMed]
49. Huang Q, Yin W, Chen X, Wang Y, Li Z, Du S, Wang L, Shi C. Nanotheranostics. 2018;2:21. doi: 10.7150/ntno.22091. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
50. Akbarzadeh A, Samiei M, Davaran S. NANOSCALE RES LETT. 2012;7:144. doi: 10.1186/1556-276X-7-144. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
51. Powell AA, Talasaz AH, Zhang H, Coram MA, Reddy A, Deng G, Telli ML, Advani RH, Carlson RW, Mollick JA, Sheth S, Kurian AW, Ford JM, Stockdale FE, Quake SR, Pease RF, Mindrinos MN, Bhanot G, Dairkee SH, Davis RW, Jeffrey SS. PLOS ONE. 2012;7:e33788. doi: 10.1371/journal.pone.0033788. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
52. Talasaz AH, Powell AA, Huber DE, Berbee JG, Roh KH, Yu W, Xiao W, Davis MM, Pease RF, Mindrinos MN, Jeffrey SS, Davis RW. Proc Natl Acad Sci U S A. 2009;106:3970. doi: 10.1073/pnas.0813188106. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
53. Peng YY, Hsieh TE, Hsu CH. Journal of Nanoscience & Nanotechnology. 2009;9:4892. doi: 10.1166/jnn.2009.1102. [PubMed] [CrossRef] [Google Scholar]
54. Wu C, Schneider T, Zeigler M, Yu J, Schiro PG, Burnham DR, McNeill JD, Chiu DT. J AM CHEM SOC. 2010;132:15410. doi: 10.1021/ja107196s. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
55. Li K, Hong E, Wang B, Wang Z, Zhang L, Ruixia H, Wang B. Photodiagnosis Photodyn Ther. 2018. [Google Scholar]
56. Shen J, Li K, Cheng L, Liu Z, Lee ST, Liu J. ACS Appl Mater Interfaces. 2014;6:6443. doi: 10.1021/am405924g. [PubMed] [CrossRef] [Google Scholar]
57. Bajaj A, Miranda OR, Kim IB, Phillips RL, Jerry DJ, Bunz UH, Rotello VM. Proc Natl Acad Sci U S A. 2009;106:10912. doi: 10.1073/pnas.0900975106. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
58. Nagesetti A, Rodzinski A, Stimpf E, Stewart T, Khanal C, Wang P, Guduru R, Liang P, Agoulrik I, Horstmyer J, Khizroev S. Sci Rep. 2017;7:1610. doi: 10.1038/s41598-017-01647-x. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
59. Schneek, H.; Gierke, B.; Uppenkamp, F.; Behrens, B.; Niederacher, D.; Stoecklein, N. H.; Templin, M. F.; Pawlak, M.; Fehm, T.; Neubauer, H., PLOS ONE, (2015) 10, e144535. [PMC free article] [PubMed]
60. Chen, L.; Peng, M.; Li, N.; Song, Q.; Yao, Y.; Xu, B.; Liu, H.; Ruan, P., Sci Rep, (2018) 8, 1188. [PMC free article] [PubMed]
61. Wang, D.; Wu, L.; Liu, X., ADV EXP MED BIOL, (2017) 994, 275. [PMC free article] [PubMed]
62. Li, H.; Meng, Q. H.; Noh, H.; Somaiah, N.; Torres, K. E.; Xia, X.; Bath, I. S.; Joseph, C. P.; Liu, M.; Wang, R.; Li, S., ONCOIMMUNOLOGY, (2018) 7, e1420450. [PMC free article] [PubMed]
63. Satelli, A.; Bath, I.; Brownlee, Z.; Mitra, A.; Zhou, S.; Noh, H.; Rojas, C. R.; Li, H.; Meng, Q. H.; Li, S., Oncotarget, (2017) 8, 49329. [PMC free article] [PubMed]
64. Satelli, A.; Mitra, A.; Cutrera, J. J.; Devarie, M.; Xia, X.; Ingram, D. R.; Dibra, D.; Somaiah, N.; Torres, K. E.; Ravi, V.; Ludwig, J. A.; Kleinerman, E. S.; Li, S., CANCER RES, (2014) 74, 1645. [PMC free article] [PubMed]
65. Satelli, A.; Bath, I. S.; Brownlee, Z.; Rojas, C.; Meng, Q. H.; Kopetz, S.; Li, S., Sci Rep, (2016) 6, 28910. [PMC free article] [PubMed]
66. Pal, S. K.; He, M.; Chen, L.; Yang, L.; Pillai, R.; Twardowski, P.; Hsu, J.; Kortylewski, M.; Jones, J. O., Urol Oncol, (2018) 36, 161. [PMC free article] [PubMed]
67. Lee, H. M.; Joh, J. W.; Seo, S. R.; Kim, W. T.; Kim, M. K.; Choi, H. S.; Kim, S. Y.; Jang, Y. J.; Sinn, D. H.; Choi, G. S.; Kim, J. M.; Kwon, C.; Chang, H. J.; Kim, D. S.; Ryu, C. J., Sci Rep, (2017) 7, 13201. [PMC free article] [PubMed]
68. Okumura T, Yamaguchi T, Watanabe T, Nagata T, Shimada Y. Methods Mol Biol. 2017;1634:211. doi: 10.1007/978-1-4939-7144-2_18. [PubMed] [CrossRef] [Google Scholar]
69. Liu, S.; Tian, Z.; Zhang, L.; Hou, S.; Hu, S.; Wu, J.; Jing, Y.; Sun, H.; Yu, F.; Zhao, L.; Wang, R.; Tseng, H. R.; Zhau, H. E.; Chung, L. W.; Wu, K.; Wang, H.; Wu, J. B.; Nie, Y.; Shao, C., Oncotarget, (2016) 7, 59877. [PMC free article] [PubMed]
70. Kuhlmann, J. D.; Wimberger, P.; Bankfalvi, A.; Keller, T.; Scholer, S.; Aktas, B.; Buderath, P.; Hauch, S.; Otterbach, F.; Kimmig, R.; Kasimir-Bauer, S., CLIN CHEM, (2014) 60, 1282. [PubMed]
71. Seferos DS, Giljohann DA, Hill HD, Prigodich AE, Mirkin CA. J AM CHEM SOC. 2007;129:15477. doi: 10.1021/ja0776529. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
72. Choi CH, Hao L, Narayan SP, Auyeung E, Mirkin CA. Proc Natl Acad Sci U S A. 2013;110:7625. doi: 10.1073/pnas.1305804110. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
73. Briley WE, Bondy MH, Randeria PS, Dupper TJ, Mirkin CA. Proc Natl Acad Sci U S A. 2015;112:9591. doi: 10.1073/pnas.1510581112. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

74. Seftor EA, Seftor R, Weldon D, Kirsammer GT, Margaryan NV, Gilgur A, Hendrix M. SEMIN ONCOL. 2014;**41**:259. doi: 10.1053/j.seminoncol.2014.02.001. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
75. Halo TL, McMahon KM, Angeloni NL, Xu Y, Wang W, Chinen AB, Malin D, Strekalova E, Cryns VL, Cheng C, Mirkin CA, Thaxton CS. Proc Natl Acad Sci U S A. 2014;**111**:17104. doi: 10.1073/pnas.1418637111. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
76. Lee K, Cui Y, Lee LP, Irudayaraj J. NAT NANOTECHNOL. 2014;**9**:474. doi: 10.1038/nnano.2014.73. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
77. Bertrand N, Wu J, Xu X, Kamaly N, Farokhzad OC. Adv Drug Deliv Rev. 2014;**66**:2. doi: 10.1016/j.addr.2013.11.009. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
78. Golombek SK, May JN, Theek B, Appold L, Drude N, Kiessling F, Lammers T. Adv Drug Deliv Rev. 2018;**130**:17. doi: 10.1016/j.addr.2018.07.007. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
79. Matsumura, Y.; Maeda, H., CANCER RES, (1986) 46, 6387. [PubMed]
80. Hong, G.; Robinson, J. T.; Zhang, Y.; Diao, S.; Antaris, A. L.; Wang, Q.; Dai, H., Angew Chem Int Ed Engl, (2012) 51, 9818. [PubMed]