Journal of Science and Technology
ISSN: 2456-5660 Volume 06, Issue 02, March-April 2021
www.jst.org.in DOI: https://doi.org/10.46243/jst.2021.v6.i2.pp17-22

Distinctiveness of Nanoparticles Drug Delivery in Cancer

Dr. A. Mohamed Sikkander[1], Dr. K. Kavitha[2], Ms. S. Sasikala[3], Dr. Khadeeja Yasmeen[4]

[1]*(Department of Chemistry, Velammal Engineering College, Chennai-INDIA)*
[2]*(Department of Chemistry, Velammal Engineering College, Chennai-INDIA)*
[3]*(Department of Chemistry, Velammal Engineering College, Chennai-INDIA)*
[4]*(Department of Biotechnology, North East Frontier Technical University, Arunachal Pradesh-INDIA)*
[1]*Corresponding Author: ams240868@gmail.com*

To Cite this Article
Dr. A. Mohamed Sikkander, Dr. K. Kavitha, Ms. S. Sasikala, Dr. Khadeeja Yasmeen, "Distinctiveness of Nanoparticles Drug Delivery in Cancer", Journal of Science and Technology, Vol. 06, Issue 02, March-April 2021, pp17-22

Article Info
Received: 22-11-2020 Revised: 15-01-2021 Accepted: 28-01-2021 Published: 03-02-2021

Abstract: *Nanomedicine is the effect of advances in Nanoscience and nanotechnology and is normally referred to as biotechnology applications in Nanoscience and nanotechnology. Also, the Nanomedicine development of fields of analysis and treatment in biological systems at the cellular and sub-cellular levels has provided revolutionary methods for the recognition and deterrence of certain fatal diseases. For example, the National Cancer Institute of America expects nanotechnology and Nanoscience to be used to manage cancer and thus reduce mortality. Because of the closeness of Nanoscience to fertility, the US Department of the Food and Drug direction has been exploring the complex issues associated with nanoscale testing, nanoparticles, and Nanosystems to get better human life. Nanoscale resources can be described as a range of atoms up to 100 nanometers, and almost a nanoscale substance is defined as a material with the smallest dimensions of less than 100 nanometers.*

Keywords*: Avascular Tumor, Cancer diagnosis, Drug Delivery, Nanomedicine, Vascular Tumor.*

I. Introduction

Nanomaterials have only one of its kind properties compared to larger ones, and sometimes the nanoscale range can boost to 1,000 nm. The far above the ground tendency to design non-biological Nano-materials is due to their exact functions and the properties of nanoscale biological materials. At the same time, nanoscale materials can be used to access or maneuver non-biological Nanomaterials for the reason that they have the right size (1). Nanomaterials that are less than 50 nm in size do not have the difficulty of entering many cells, while Nanomaterials which are smaller than 20 nm can move further than the blood vessels and move around the body's circulatory system. Therefore, after particular treatments, Nanomaterials are widely used as drug delivery systems whose position is to transfer chemotherapeutic materials or therapeutic genes to malignant cells, while defensive healthy cells and store them. As a momentous note it can be said that, in numerous practical sections of literature, nanomaterials are commonly called as non-biological nanomaterials, however, in the preparation and invention of nonbiological nanomaterials, organisms and biological methods have been extraordinarily used (2).

One of the reasons for the appearance of nanotechnology is the unforeseen knowledge-based and technical development in miscellaneous areas, such as pharmacy and biomedicine. One nanometer can be described as one billionth of a meter and three times slighter than micron (3). Over the past a small number of years, nanotechnology has been instrumental in the field of medicine and its development. Studies show that a wide range of Nanomaterials has emerged that have biomedical applications such as skin ulcer healing, bone tissue engineering, and smart drug delivery systems . Smart drug delivery systems relate to triumphant and inclusive examples of Nanomaterials with far above the ground potential for imaging, sensitivities, or therapies. Over the past decade, nanoscale resources have been reported with a good drug delivery capability and cancer treatment ability.

II. Nanotechnologies in medicine

Molecular nanotechnology is fashioned on the measurement scale in which it operates. It indicates hundreds or thousands of nanometers (4). It can be well thought-out that 3 or 4 atoms are present in a nanometer. In nanotechnology, the size of viruses can be tacit as 100 nanometers. Also, the diameter of human hair is measured as almost 200 µm. Atom can be considered as the main element of molecular nanotechnology structure. The uniqueness of the product result such as tension, conductance or power is enhanced by groups of atoms. Adaptation of graphite into the strong and hard structure of diamond is a clear example of this process. Also, reorganization and improvement of sand atoms can lead to the formation of a medium silicone plate for edifice semiconductor devices. Therefore, physicochemical conditions and biotic elements of these nanostructures can be helpful for improvement of biomedical applications (5). If inclusive efforts are made for developing nanotechnology and its completion, it is possible to make the world a safer place for living. So, the sensors obtainable in the industry are not expelled from this rule. In the earlier period, nanosensors have been used for conducting researches.

A nanosensor can be defined as a sensor that is built on an atomic scale which is based on nanometer measurements. Advancement and assessment of nanosensors can be observed in applications such as medicine, native safety, aerospace, combined circuit, etc. In adding up to the variety of distinct usage for nanosensors, there are different kinds of nanosensors and dissimilar methods for preparing and producing them. There are challenges for edifice of these nanosensors. However, they get advanced and improved for regular use, their advantages are greater than before and their role in daily schedule in enhances. The reason of nanosensors can be mainly considered as achieving in sequence on a nuclear scale and transferring them to the information which can be simply inspected. Using nanocomponents, more often than not in microscopic or submicroscopic scales, such sensors can be known as "physical or chemical sensors". One of the distinctiveness of these particles is their powerful sensitivity. So, they have the capacity of identifying subatomic of viruses or indeed very low concentrations of the material which is naturally detrimental.

Nanotechnology usually has the facility to design and controlling a nano-size object. However, according to the researchers' opinions, it can be said that they have diverse ideas about nanotechnology, and it seems that definitions of nanotechnology are also speckled as its applications (6). Some people have paying attention on the study of microstructure materials by an electron microscope and formative narrow sheets as nanotechnology. A number of others have investigated the synthesis method and edifice materials as nanotechnology. Protein system, which is a nanotechnology, is defined as a set for protein delivery to a precise position in the body. The above definitions have meanings in exact research areas, but none of them drape the whole range of nanotechnology. In view of the fact that nanotechnology covers a wide range of research areas and requires interdisciplinary and multidisciplinary efforts, dissimilar definitions have been proposed for nanotechnology. According to the concepts and definitions of nanotechnology, it can be incidental that the only widespread feature of nanotechnology is its small size. In common, nanotechnology is measured as a technology for designing, building, and using nanomaterials and nanostructures. Nanotechnology covers the essential understanding of physical properties and nanomaterial and nanostructure fact and includes the fundamental study of the relationship between physical properties and the size of materials in nanometer scale. In order to suggest a comprehensive definition, nanotechnology is associated to materials and systems whose structure and components are new and their biological, chemical and physical properties are appreciably developed. This can be conveying to nanoparticle size. Although the term "nanotechnology" is novel, the study of nanometer scale is not impressive new. It is accepted that, the research of biological systems and engineering of numerous materials such as colloidal dispersion metal quantum dots and catalysts have existed for several years (7).

Development and advancement of devices such as transmission electron microscopy (TEM), scanning tunneling microscopy (STM), and scanning probe microscope (SPM) have been used for developing novel facilities for specifying, measuring and manipulating nanomaterials and nanostructures. So, it can be affirmed that by using these tools, it is probable to study and manipulate nanomaterials and nanostructures at atom level. Iron-reducing bacteria (IRB) can be introduced as one of the majority favorable microorganisms that present in different industrial and environmental activities. The facility of IRB to build iron nanostructures has made the bacteria fascinating in nanobiology technology(8). According to modern studies, it can be stated that these materials can also be used as nanosensors, countless application can be considered for them.

III. Nanobiosensor in cancer diagnosis

Cancer is one of the majority leading cause of death worldwide and can take over 200 diverse forms, including lung, prostate, breast, cervical, ovarian, hematologic, colon cancer, and leukemia(9). It has been originate

that environmental factors as well as genetic factors are connected with an increased threat in the expansion and progression of cancer. In addition microorganisms are also reported to be connected with some types of cancer. In view of such an imperative medical condition, quite a lot of methods have already been discovered to diagnose cancer and a lot of methods are in the process of development. Conservative clinical approaches to detect cancers are based on biopsy followed by histopathology, biomarkers using protein levels or nucleic acid content and its appearance in the cancer suspects (10). Biopsy is the most widely used technique; however, it is a persistent technique and cannot always be used. In addition to that, it cannot be applied when cancer biomarkers are there in awfully low concentrations in the body fluids and in malignant tissues. Expansion of highly sensitive and innovative techniques of cancer diagnosis is really interesting and significant in medical science. Due to high importance in interdisciplinary research in the previous decade several nanobiosensors based on **spectrophotometric** or optical methods, fluorescence immunoassay, chemiluminescence analysis, electrochemistry, radioimmunoassay, capillary electrophoresis and chromatographic analysis have been urbanized to perceive cancer biomarkers (proteomic and genetic markers) and cells(11). The chief issues in cancer diagnosis are sensitivity and to develop miniaturized platforms that can be used as point-of-care medical device and can be functionalized in the remote areas. The expansion of electrochemical nanobiosensors composed of nanomaterials and biological receptors are likely the most encouraging approach to solve the troubles associated to sensitivity, rapidity, selectivity, and low cost. This comes up to is expected to be very effectual for cancer diagnosis due to the combination of conventional bioassay coupled with nanomaterials and electrochemical dimension. Another advantage of the electrochemical biosensor includes its ability to be miniaturized as an onsite medical device, low cost, small, and handy size. These features of electrochemical **nanobiosensors** possibly will serve as a smart substitute to support fast cancer diagnosis, by this means designing better therapeutic strategies which will be awfully helpful in decreasing patient stress (12).

Frequently an electrochemical nanobiosensor is developed for either cancer biomarkers detection for example; embryonic antigen biomarkers, carbohydrate antigens biomarkers, enzyme and isozyme **biomarkers**, protein biomarkers, hormone biomarkers etc (13). The real implication of all these studies is to develop at first a sensor prototype and then interpret it into a genuine and real biomedical device for cancer suspects and patients.

A current electrochemical nanobiosensor for breast cancer diagnosis has been developed,where in a single prototype human epidermal growth factor receptor 2 (HER2) protein and HER2-overexpressing **breast cancer** cells have been detected by an electrochemical nanobiosensor unswervingly in body fluids. The sensor probe was fictitious by covalently immobilizing anti-HER2 onto a nanoconducting film and the signal was obtained by a narrative bio conjugate self-possessed of hydrazine−gold nanoparticle−aptamer, where the hydrazine acted as an electro catalyst and aptamer worked as a reporter molecule. The urbanized sensor was capable of differentiate between HER2-positive breast cancer cells and HER2-negative cells. This technique exhibited an excellent diagnosis technique for the ultrasensitive detection of SK-BR-3 breast cancer cells in real samples (14). The interesting characteristic of this method is that, it is a generic technique and can be applied for any type of cancer biomarkers and cells merely by changing the detector and reporter probe. In one more study, a voltammeric and impidimetric detection of microRNA-21 and mir-21 from cell lysates was investigated for the finding of breast cancer cell line and hepatoma cell line .The developed biosensor showed detection limit of 2.09µg/mL and was efficiently applied in real sample analysis. Apart of cancer diagnosis based on independently analyte detection, multiplex detection strategies have also been attempted by various research groups. In this gaze at, an electrochemical detector has been included with the microfluidic system for the simultaneous detection of cancer protein markers. For instance, reported an integrated microfluidic system for the electrochemical finding of breast cancer markers unswervingly in patient serum samples (15). The outcome obtained in this particular case were in outstanding correlation with the conventionally used ELISA method indicating the assure of microfluidic integrated electrochemical sensor for multiplex detection of cancer biomarkers.

IV. Cancer and Drug Delivery

Cancer is an unrestrained disease but its providence is still undecided. No doubt in the last not many decades scientists have shown the advancement to defeat this disease but are still not able to eliminate cancer from society.

Table no 1: Tumour Type

Vascular Tumor	Avascular Tumor
50% Cells	Sooner than blood vessels
10% Blood vessels	Nutrient obtained via diffusion
40% Extra cellular matrix	Cells in the center be malnourished
Vessel structure is not organized	Cells on the fringe increase
May be benign and encapsulated or malignant	Cells in the interior are dormant, Growth limited to a small

	number of mm in diameter

Tumor blood vessels have more than a few abnormalities compared with physiological vessels like relatively high quantity of proliferating endothelium cells, an increased tortuosity and an aberrant crypt membrane formation(16). The speedily increasing tumor vasculature often has discontinuous endothelium, with gaps between the cells that may be more than a few hundred nanometres large.

Macromolecular transport pathways transversely tumor vessels occur via open gaps, vesicular vacuolar organelles and fenestrations. However it remains controversial which pathways are chiefly responsible for hyperpermeability and macromolecular transvascular transport.

Tumor interstitial is also characterized by a high interstitial pressure, leading to an outward convective interstitial fluid flow, as well as the nonattendance of an anatomically well defined implementation lymphatic network. Physiological barriers at the tumor level (i.e., poorly vascularized tumor regions, acidic environment, elevated interstitial pressure and squat microvascular pressure) as well as the cellular level (i.e., tainted activity of specific enzyme systems, altered apoptosis regulation and transport based mechanism) and in the body (i.e., allocation, biotransformation and consent of anticancer agent) must be overcome to delivery anticancer agents to tumor cells in vivo.

Extremely slow, time-consuming development in the treatment of severe diseases has led to the espousal of a multidisciplinary move toward to the targeted delivery and release of drugs, underpinned by nanoscience and nanotechnology (17).

Drug carriers embrace micro and nanoparticles, micro and nanocapsules, lipoproteins, liposomes, and micelles, which can be engineered to slowly degrade, act in response to stimuli and be site-specific. The eventual aim is to minimize drug degradation and loss, prevent harmful side effects and increase the ease of use of the drug at the disease site.

Chemotherapy via Nanoparticles

Chemotherapy by means of nanoparticles has been studied in clinical trials for several years and lots of studies have been available in this regards. Nanoscale drug delivery systems for chemotherapy can be alienated into two categories: Polymer and lipid based. Polymer based nanoparticles are more successful (18).

Nanoparticles and Their Role in Cancer

Nanoparticles play an extremely important role in cancer research. Nanoparticles are steady, solid colloidal particles consisting of biodegradable polymer or lipid materials and range in size from 10 to 1,000 nm.Nanotechnology has incredible potential to make an important contribution in cancer prevention, detection, diagnosis, imaging and treatment.

Nanoparticles have payback because of its size. Because of their size they can without difficulty enter small places. Nanoparticles have paying attention of scientists because of their multifunctional character. Nanoparticles have large surface area to volume ratio, that helps in diffusion also most important to special properties such as increased heat and chemical resistance.

Transportation of Oxygen, Nutrient & Nanoparticles within Tumor

The preponderance of the ~1013 cells in the human body is within a few cell diameters of a blood vessel. This notable feat of organization facilitates the delivery of oxygen and nutrients to the cells that form the tissue of the body. It also enables the well-organized delivery of most medicines. As a result of inadequately organized vasculature in solid tumors, there is limited delivery of oxygen and other nutrients to cells that are far-off from functional blood vessels (19).

A single cancerous cell together with this by healthy tissue will replicate at a rate higher than the other cells, placing a strain on the nutrient deliver and removal of metabolic waste products (20). Once a diminutive tumor mass has formed, the healthy tissue will not be able to fight with the cancer cells for the inadequate provider of nutrients from the blood stream. Tumor cells will be in motion healthy cells until the tumor reaches a diffusion-limited maximal size. While tumor cells will classically not begin apoptosis in a low nutrient environment, they do necessitate the normal building blocks of cell function like oxygen, glucose and amino acids. The vasculature was intended to supply the now extinct healthy tissue that did not place as high a demand for nutrients due to its slower growth rate. Tumor cells will therefore persist dividing because they do so without regard to nutrient supply but also many tumor cells will die since the amount of nutrients is not enough (21). The tumor cells at the external edge of a mass have the best access to nutrients while cells on the inside die creating a necrotic core inside tumors that rely on diffusion to deliver nutrients and take away waste products.

In core, a steady state tumor size forms, as the rate of propagation is equal to the rate of cell death until a better association with the circulatory system is created. Active tumor targeting of nanoparticles involves attaching molecules recognized as a group as ligands, to the outsides of nanoparticles. These ligands are astonishing in that

they can recognize and bind to harmonizing molecules, or receptors, found on the surface of tumor cells. When such targeting molecules are added to a drug delivery nanoparticle, additional of the anticancer drug finds and enters the tumor cell, increasing the competence of the treatment and reducing toxic effects on surrounding usual tissue (22). Dissimilar types of nanoparticles are developed to deliver drug at target site (Fig: 1).

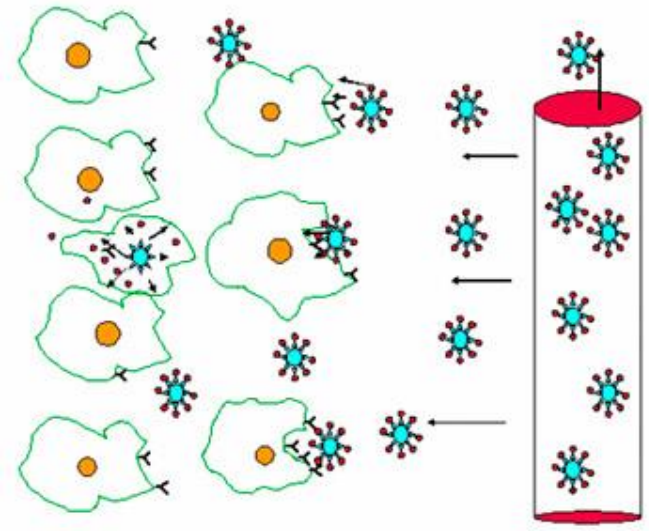

Figure no 1: The ligands on the facade of the nanoparticles fit into the cell receptors, allowing encapsulated drug molecules to go through the tumor cell after binding.

Nanoparticles and additional nanostructures come into view to hold great promise for the future of cancer treatment. Distinctiveness of nanoparticles for cancer drug delivery are given below:

Table no 2: Distinctiveness of nanoparticles worn for cancer drug delivery

Structure	Size	Role in drug Delivery
Carbon magnetic Nanoparticles	40-50 nm	For drug delivery and targeted cell demolition
Dendrimers	1-20 nm	Asset therapeutic substances such as DNA in their cavities
Liposomes	20-25 nm	A novel cohort of liposomes that incorporate fullerenes to deliver drug that are not water soluble, that tend to have large molecules
Low Density Lipoprotein	20-25 nm	Drug solublized in the lipid core or fond of to the surface
Nanolipispheres	25-50 nm	Carrier inclusion of lipophilic and hydrophilic drugs
Nanoparticles	25-200 nm	Act as incessant matrices containing dispersed or dissolved drug
Nanospheres	50-500 nm	Hollow ceramic nanospheres fashioned by ultrasound
Nanovesicles	25-3000 nm	sole or bilayer spheres containing the drugs in lipids
Polymer Nanocapsules	50-200 nm	worn for enclosing drugs

V. Conclusion

The beginning of nanomedicines represents significant advances in the field of drug delivery. The options for nanoparticle intend and function is tremendously speckled and the list of probable applications continues to grow, to the point where the drug delivery system can be made to measure to best suit the selected drug. However, it is significant to retain information that nanoparticle-based treatments are not wonder cures. They have in cooperation flaws and challenges to overcome. Choosy targeting, while heralded as an development over non-encapsulated drugs, is a confront unto itself. While a lot of cancers over express surface proteins general in normal cells, superfluity of a specific surface protein is not adequate to guarantee selectivity by means of targeted treatment. Eventually, some of the drug will end up off-target, affecting non-cancerous cells. Choosing the exact surface marker is critical for a targeted treatment to work. For liposomal irinotecan, selectivity is achieved from beginning to end the acidic tumor microenvironment.

References

[1]. Physicochemical Properties of Nanomaterials: Implication in Associated Toxic Manifestations, Manzoor Ahmad Gatoo, Sufia Naseem, Mir Yasir Arfat, Ayaz Mahmood Dar, Khusro Qasim, and Swaleha Zubair, Toxicity of Nanomaterials, Volume 2014 |Article ID 498420 | 8 pages | https://doi.org/10.1155/2014/498420

[2]. Review on nanoparticles and nanostructured materials: history, sources, toxicity and regulations,Jaison Jeevanandam, Ahmed Barhoum, Yen S Chan, Alain Dufresne, and Michael K Danquah, Beilstein J Nanotechnol. 2018; 9: 1050–1074. Published online 2018 Apr 3. doi: 10.3762/bjnano.9.98

[3]. Effects of Local Application of Nano-silver on Osteomyelitis and Soft Tissue Infections: An Eximental Study in Rats, Bahattin Kemah,Gökçer Uzer,yalçın Turhan,Korhan Özkan, Journal of Bone and Joint Infection 3(1):43-49, April 2018, DOI: 10.7150/jbji.22121

[4]. Nanotools for Neuroscience and Brain Activity Mapping,A. Paul Alivisatos, Anne M. Andrews, Edward S. Boyden, Miyoung Chun, George M. Church, Karl Deisseroth, John P. Donoghue, Scott E. Fraser, Jennifer Lippincott-Schwartz, Loren L. Looger, Sotiris Masmanidis, Paul L. McEuen, Arto V. Nurmikko, Hongkun Park, Darcy S. Peterka, Clay Reid, Michael L. Roukes, Axel Scherer, Mark Schnitzer, Terrence J. Sejnowski, Kenneth L. Shepard, Doris Tsao, Gina Turrigiano, Paul S. Weiss, Chris Xu, Rafael Yuste, and Xiaowei Zhuang, ACS Nano. 2013 Mar 26; 7(3): 1850–1866.Published online 2013 Mar 20. doi: 10.1021/nn4012847

[5]. Biomedical Applications of Silver Nanoparticles: An Up-to-Date Overview,Alexandra-Cristina Burdușel, Oana Gherasim, Alexandru Mihai Grumezescu, Laurențiu Mogoantă, Anton Ficai, and Ecaterina Andronescu, Nanomaterials (Basel). 2018 Sep; 8(9): 681. Published online 2018 Aug 31. doi: 10.3390/nano8090681

[6]. Nanotechnology in cosmetics: Opportunities and challenges,Silpa Raj, Shoma Jose, U. S. Sumod, and M. Sabitha, J Pharm Bioallied Sci. 2012 Jul-Sep; 4(3): 186–193. doi: 10.4103/0975-7406.99016

[7]. Nanoparticles: Properties,applications and toxicities, lIbrahimKhan, KhalidSaeed, IdreesKhan, Arabian Journal of Chemistry,Volume 12, Issue 7, November 2019, Pages 908-931,doi.org/10.1016/j.arabjc.2017.05.011

[8]. Iron-Reducing Bacteria and Iron Nanostructures,Alireza Ebrahiminezhad , Zahra Manafi , Aydin Berenjian, Sedigheh Kianpour , Younes Ghasemi ,Fasa University of Medical Sciences, Volume 3, Issue 1,March 2017,Pages 9-16,doi.org/10.18869/NRIP.JAMSAT.3.1.9

[9]. Incidence and death in 29 cancer groups in 2017 and trend analysis from 1990 to 2017 from the Global Burden of Disease Study,Longfei Lin, Lei Yan,Yuling Liu, Fang Yuan,Hui Li and Jian Ni,Journal of Hematology & Oncology volume 12, Article number: 96 (2019)

[10]. Blood-Based Cancer Biomarkers in Liquid Biopsy: A Promising Non-Invasive Alternative to Tissue Biopsy José Marrugo-Ramírez, Mònica Mir, and Josep Samitier, Int J Mol Sci. 2018 Oct; 19(10): 2877. doi: 10.3390/ijms19102877

[11]. Electrochemical Nanobiosensors for Cancer Diagnosis, Pranjal Chandra, Journal of Analytical & Bioanalytical Techniques 6(2), April 2015, DOI: 10.4172/2155-9872.1000e119

[12]. Biosensors: the new wave in cancer diagnosis,Brian Bohunicky and Shaker A Mousa, Nanotechnol Sci Appl. 2011; 4: 1–10. doi: 10.2147/NSA.S13465

[13]. Electrochemical Biosensors for Determination of Colorectal Tumor Biomarkers,Jennifer Quinchia, Danilo Echeverri, Andrés Felipe Cruz-Pacheco, María Elena Maldonado, and Jahir Orozco, Micromachines (Basel). 2020 Apr; 11(4): 411. doi: 10.3390/mi11040411

[14]. HER 2: Biology, Detection, and Clinical Implications, Carolina Gutierrez, and Rachel Schiff, Arch Pathol Lab Med. 2011 Jan; 135(1): 55–62.doi: 10.1043/2010-0454-RAR.1

[15]. Multiplex Immunosensor Arrays for Electrochemical Detection of Cancer Biomarker Proteins, Bernard S. Munge, Thomas Stracensky, Kathleen Gamez, Dimitri DiBiase, and James F. Rusling, Electroanalysis. 2016 Nov; 28(11): 2644–2658. doi: 10.1002/elan.201600183

[16]. Why are tumour blood vessels abnormal and why is it important to know? J A Nagy, S-H Chang, A M Dvorak, and H F Dvorak, Br J Cancer. 2009 Mar 24; 100(6): 865–869.doi: 10.1038/sj.bjc.6604929

[17]. Mechanisms of new blood-vessel formation and proliferative heterogeneity of endothelial cells ,Hisamichi Naito, Tomohiro Iba, Nobuyuki Takakura,International Immunology, Volume 32, Issue 5, May 2020, Pages 295–305, https://doi.org/10.1093/intimm/dxaa008

[18]. Effective use of nanocarriers as drug delivery systems for the treatment of selected tumors,Fakhar ud Din, Waqar Aman, Izhar Ullah, Omer Salman Qureshi, Omer Mustapha, Shumaila Shafique, and Alam Zeb, Int J Nanomedicine. 2017; 12: 7291–7309. doi: 10.2147/IJN.S146315

[19]. NORMALIZATION OF THE VASCULATURE FOR TREATMENT OF CANCER AND OTHER DISEASES,Shom Goel, Dan G. Duda, Lei Xu, Lance L. Munn, Yves Boucher, Dai Fukumura, and Rakesh K. Jain, Physiol Rev. 2011 Jul; 91(3): 1071–1121. doi: 10.1152/physrev.00038.2010

[20]. Cancer nanomedicine: a review of recent success in drug delivery,Stephanie Tran, Peter-Joseph DeGiovanni, Brandon Piel, and Prakash Rai, Clin Transl Med. 2017; 6: 44. doi: 10.1186/s40169-017-0175-0

[21]. Nanoparticle-Based Photo-triggered Cancer Immunotherapy and Its Domino Effect in the Tumor Microenvironment, Santhosh Kalash Rajendrakumar, Saji Uthaman, Chong-Su Cho, and In-Kyu Park, Biomacromolecules 2018, 19, 6, 1869–1887, doi.org/10.1021/acs.biomac.8b00460

[22]. Nano based drug delivery systems: recent developments and future prospects,Jayanta Kumar Patra, Gitishree Das, Leonardo Fernandes Fraceto, Estefania Vangelie Ramos Campos, Maria del Pilar Rodriguez-Torres, Laura Susana Acosta-Torres,Luis Armando Diaz-Torres, Renato Grillo, Mallappa Kumara Swamy, Shivesh Sharma, Solomon Habtemariam, and Han-Seung Shin, J Nanobiotechnology. 2018; 16: 71.. doi: 10.1186/s12951-018-0392-8.