Vaccine Research
ISSN: 2423-4923
eISSN: 2383-2819

Carbon Nanotube-Based Nanovaccines in Lung Cancer Immunotherapy

Mojgan Sheikhpour[1,2]*, Hanie Sakhi[1]

[1]Department of Mycobacteriology and Pulmonary Research, Pasteur Institute of Iran, Tehran, Iran. [2]Microbiology Research Center (MRC), Pasteur Institute of Iran, Tehran, Iran

ARTICLE INFO

Review Article

VacRes, 2023
Vol. 10, No.2, 56 – 59
Received: December 27, 2025
Accepted: February 09, 2026
Pasteur Institute of Iran

***Corresponding Authors:**

Mojgan Sheikhpour;
Department of Mycobacteriology and Pulmonary Research, Pasteur Institute of Iran, Tehran, Iran.
Email: m_sheikhpour@pasteur.ac.ir
Tel/Fax: (+98) 21 64112285/ (+98) 21 64112313

KEYWORDS: Lung cancer, carbon nanotube, nanovaccine, immunotherapy

ABSTRACT

Conventional lung cancer therapies—including surgery, chemotherapy, and radiotherapy—are often limited by insufficient efficacy and significant adverse effects. In response, cancer immunotherapy, particularly vaccine-based approaches, has emerged as a promising strategy to improve outcomes. Carbon nanotubes (CNTs) represent a versatile nanoplatform capable of efficiently delivering antigens, adjuvants, and therapeutic agents, making them attractive candidates for nanovaccine development. This review examines the role of CNT-based nanovaccines in lung cancer immunotherapy, focusing on their mechanisms of action and therapeutic potential. Evidence indicates that CNT nanovaccines enhance antitumor immunity by promoting dendritic cell maturation, stimulating robust humoral and cellular immune responses, and reprogramming the immunosuppressive tumor microenvironment toward an immunopermissive state. Despite these promising preclinical results, clinical translation requires further optimization of CNT design and functionalization, alongside comprehensive *in vivo* evaluation of immunogenicity, biodistribution, and safety profiles. Overall, CNT-based nanovaccines hold considerable potential to advance lung cancer immunotherapy, though targeted research is needed to bridge the gap between experimental promise and clinical application.

INTRODUCTION

Lung cancer is one of the most common cancers, classified into two groups: non-small cell lung cancer (NSCLC; 80%) and small cell lung cancer (SCLC; 20%) [1]. The common cancer treatments include chemotherapy, surgery, and radiotherapy all of which pose different challenges and problems [2]. For instance, Chemotherapy drugs operate without cell type discrimination because they attack both normal cells and cancer cells, which leads to side effects such as hair loss, anemia and nausea. Radiotherapy together with surgical procedures create dangerous tissue destruction and visible damage to healthy areas that surround the treatment site. Because of these, other modes of therapy that are less invasive and more targeted were developed, including cancer vaccines [2].

The human body is designed with defense mechanisms that prevent the development of cancerous cells in the body. For instance, dendritic cells (DCs)—the most potent antigen-presenting cells (APCs)—activate the innate immune response against tumors by presenting tumor antigens via major histocompatibility complex (MHC) class I and II molecules. This process stimulates CD8+ and CD4+ T cells, respectively, enabling immune-mediated control of tumor growth [3-5]. On the other hand, the mutations that take place during the development of cancer cells and availability of abundant immunosuppressive regulatory T-cells within the tumor microenvironment (TME), enable them to escape the immune system. This can be the reason why recently, immunotherapy approaches, including the administration of cancer vaccines, have been one of the methods used in cancer treatment today [3, 4]. Cancer vaccines, just like infection vaccines, are comprised of antigens derived from cancer cells, which raise a robust immune response against cancerous cells in the whole body [3, 4, 6]. Furthermore, cancer vaccine techniques can induce long-lasting memory of T-cells against tumor cells, thus providing long-term immunity and long-term survival of patients [3, 4]. Vaccine carriers that can effectively deliver antigens to professional antigen-presenting cells and induce a strong and sustained immune response are of great importance. In this context, nanovaccines are a promising solution to enhance the immunogenicity of protein antigens. Nanoparticles can deliver antigens into the human body and activate the immune system. [5].

Carbon nanotubes (CNTs) include three types such as single-walled carbon nanotubes (SWCNTs), double-walled carbon nanotubes (DWCNTs), and multi-walled carbon nanotubes (MWCNTs) [2]. Recently, CNTs have been used in cancer diagnosis and treatment, including the delivery of tumor antigens to intracellular compartments, due to their compatibility with biological systems and unique properties. [2, 3]. Furthermore, CNTs can play the role of adjuvants, enhance the immune

[DOI: 10.52547/vacres.10.2.56]

response, and be taken up by immune cells and induce a specific protective immune response [7]. Due to the challenges of conventional therapies, including chemotherapy and radiotherapy, and in order to enhance the efficacy of immunotherapy, various studies have focused on CNTs-based nanovaccines. CNTs-based nanovaccines are able to deliver immunoadjuvant to DCs and enhance their maturation, which leads to the activation of $CD8^+$, $CD4^+$, B-cell differentiation, tumor-specific antibody production, and ultimately modulation of TME [8]. A summary is shown in Figure. 1.

Previous studies have indicated the efficacy of this system in the treatment of lung cancer. To illustrate, CNTs were effectively delivered tumor antigens and other immunoadjuvant to lung cancer cells, enhancing immunogenicity and inducing apoptosis [1, 9]. Also, studies on various cancers, such as melanoma, show that these vaccines are able to induce strong antitumor immune responses, increase survival, as well as tumor regression [10]. In breast and colorectal cancer, nanovaccines modulate the TME, increase the presence of cytotoxic T-cells, and have synergistic therapeutic outcomes by modulating the response to immune checkpoint inhibitors [10]. Moreover, the use of CpG-SWNTs improved the immune response, activated macrophages, NK cells, and microglia, and induced long-term immunity in the brain tumor model [7]. Overall, nanovaccines are a revolutionary development in cancer treatment and, despite the need for further research for optimization and clinical application, promising results have been presented in various types of cancer [10].

Due to the lack of comprehensive and thorough studies on the application of CNTs in the treatment of lung cancer, this narrative review explores the emerging role of CNTs in the use of nanovaccines in lung cancer immunotherapy. Furthermore, the challenges of clinical application and future prospects of CNTs-based nanovaccines are discussed to evaluate their potential as a next-generation therapeutic strategy for lung cancer.

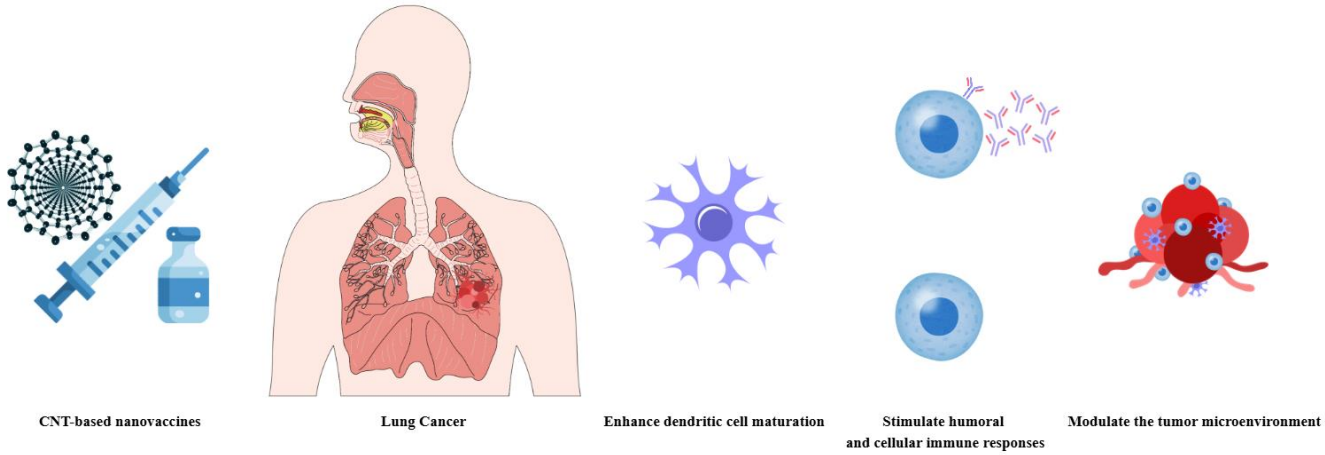

Fig 1. CNT-based nanovaccines, by delivering adjuvants, activate DCs and stimulate cytotoxic T and B cells, which can kill cancer cells directly or by producing antitumor antibodies. Finally, they modulate the TME by increasing the infiltration of immune cells into the tumor.

Literature Search Strategy

To prepare this review, a search for relevant articles from PubMed, Google Scholar, Scopus, and Since Direct databases from 2010 to 2025 was conducted using the keywords CNT, nanovaccine, lung cancer, and immunotherapy. After removing irrelevant studies, 29 articles remained, which were divided into three sections, namely, mechanism of action and induction of immune response, preclinical studies in lung cancer models, and advantages and challenges of CNT-based nanovaccines.

I- Mechanism of Action and Induction of Immune Response

Nanovaccines enhance antitumor immune responses by delivering tumor-specific antigens or antigenic peptides, activating immune cells, and modulating the TME. Besides that, nanovaccines can be loaded with adjuvants represented by agonists of TLRs, cytokines like TNF-α and IL-12, or other immune modulators capable of potent activation of APCs, resulting in endocytosis and processing of antigens with presentation on MHC molecules. This results the activation and priming of $CD8^+$ T-cells against recognition and killing of cancer cells expressing the same antigen [10]. Hassan *et al*. in 2016 [3] used MWCNTs to deliver antigen ovalbumin and two immune adjuvants (CpG and αCD40) which demonstrated improved cancer immunotherapy results and tumor growth suppression. Conjugates designed to co-deliver antigens and adjuvants to dendritic cells (DCs) can more effectively induce cytotoxic T lymphocyte (CTL) responses and promote antitumor immunity [11]. Since the TME is immunosuppressive, nanovaccines can contain agents such as regulatory T-cells and myeloid-derived suppressor cells that target immunosuppressive cells. The antitumor response becomes more powerful when nanovaccines eliminate suppressor cells from the body. In addition, some nanovaccines can increase the penetration of immune cells into the tumor and improve immune surveillance and recognition of cancer cells [10]. Therefore, enhanced antigen presentation and T-cell priming are promising for targeting poorly immunogenic tumors such as NSCLC in order to break immune tolerance.

II- Preclinical Studies in Lung Cancer Models

The study by Villa *et al.* [9] showed that SWNTs can serve as effective carriers for weak tumor antigens in lung cancer. By binding Wilms tumor protein, which is overexpressed in lung cancers, to SWNTs, they were taken up by APCs and induced a strong and specific IgG antibody response [9]. In 2025 [1], Sheikhpour *et al* used polyethylenimine-functionalized MWCNT as a nanodelivery system for microRNA-146a to A549 lung cancer cells, which targeted the TNF receptor associated factor (*TRAF6)* gene through the NF-κB pathway. This system increased apoptosis and decreased expression of *BCL-2*, *IL-6*,

[DOI: 10.52547/vacres.10.2.56]

and *TNF-α* genes. Another study showed that CNTs are intrinsically able to act as adjuvants by activating the innate immune system and inducing inflammatory cytokines such as *IL-6*, *TNF-α*, and *IL-1β* [7]. These mechanisms provide evidence of the outstanding potential of CNTs as a promising carrier in therapeutic vaccine and immunotherapy strategies in lung cancer with the aim of inducing programmed cell death of cancer cells and modulating the inflammatory response [12]. Several studies have confirmed the potential of CNTs as efficient carriers in lung cancer immunotherapy. Cationic MWCNT (MWCNT-NH_3^+) can effectively deliver small interfering RNA (siRNA) to tumor cells, which inhibits the *PLK1* gene, induces apoptosis, and increases survival in animal models [13]. These findings, alongside studies reporting the ability of CNTs in dual targeting and simultaneous drug and gene delivery, highlight the prominent role of these nanostructures in the development of novel lung cancer vaccines based on RNA mechanisms and inhibition of tumor antigens [13]. Coccini *et al.* [14] found that highly functionalized MWCNT (MWCNT-NH_2) have desirable properties, including water solubility, high dispersibility, and low tendency to aggregate, and are less toxic than unfunctionalized or crude nanotubes. These nanotubes, even at relatively high doses (100 µg/ml), only cause a modest reduction in the viability of A549 lung cells. In contrast, poorly functionalized CNTs tend to aggregate and form large aggregates, leading to false-positive responses in standard cytotoxicity assays such as MTT and to unwanted inflammatory responses in lung tissue [14]. In Madkour's study [15], C57BL/6 mice were infected intravenously with OVA-expressing B16F10 melanoma cells to induce metastatic-like tumors in the lung. They were then treated with a CNT-based nanovaccine (S–/+(OVA–CpG)) as well as a more advanced formulation containing αCD40 as a second adjuvant. The results showed that these vaccines significantly reduced tumor growth in the lung and reduced lung weight, indicating the induction of a strong immune response against lung tumors [15]. CNTs, together with other nanocarriers such as polymeric nanoparticles, liposomes, and gold nanoparticles, have been proposed as promising delivery systems for DNA vaccines [16]. Moreover, lung cancer-specific antigens like tumor-associated antigens (TAAs), tumor-specific antigens (TSAs), and adjuvants such as cytokines, TLRs, and stimulator of interferon genes (STING represents an ideal approach to be loaded onto CNTs [16, 17]. Therefore, functionalized CNTs as antigen carriers which serve as fundamental tools to create lung cancer vaccines that reduce toxicity while improving safety and effectiveness.

III- Advantages and Challenges

Nanoparticles in nanovaccines increase their uptake and processing by APCs, resulting in higher immune responses and efficacy.[18-21]. This leads to better maturation of APCs and cross-presentation of antigen on MHC class I to cytotoxic $CD8^+$, which is essential for killing cancer cells [10]. Furthermore, the size of nanoparticles has a direct impact on their uptake, tumor vascular permeability, and nanovaccine efficacy. For instance, smaller nanoparticles (20–30 nm) are endocytosed by DCs and can be degraded and excreted via exocytosis [10, 21, 22]. Positively charged nanoparticles show higher uptake efficiency by APCs because of the electrostatic interaction with negatively charged cell membranes, and help to escape from lysosomes [10].

Compared to conventional vaccines, nanovaccines induce a stronger and longer-lasting immune response by carrying, delivering, and releasing antigen and adjuvants over a sustained period of time [10]. An important advantage of nanovaccines is their specific ability to simultaneously deliver antigen and adjuvant to lymph nodes and protect those molecules from degradation [18-21]. Other advantages of this technology include the possibility of lower doses, more precise targeting, improved antigen delivery, increased cytokine production, and induction of long-lasting humoral and cellular immune responses [18-24].

CNTs are capable of biodegradation by various enzymes in neutrophils and macrophages, like myeloperoxidase. This procedure involves the attack and degradation of the nanotube walls by the reactive oxygen species (ROS) being produced into substances such as carbon dioxide [21]. Due to their needle-like structure and long length, unfunctionalized CNTs are not completely phagocytosed by pulmonary macrophages and can be toxic, accumulate in the lung, cause pulmonary inflammation, fibrosis, and granuloma formation upon inhalation or systemic administration [25, 26]. CNTs induce fibrogenic differentiation in the lungs by inducing myofibroblast differentiation, which causes interstitial, bronchial, and pleural fibrosis, characterized by excessive deposition of collagen fibers and scarring of the involved tissues [25]. Also, these nanomaterials can cause severe oxidative stress and provide a suppressive environment for the immune system by damaging DNA and inducing proinflammatory pathways [27, 28]. Therefore, their appropriate functionalization with suitable polymers or biomolecules improves solubility and biocompatibility, reduces toxicity, and are gradually excreted in urine and feces [29]. Raw CNT may inadvertently induce immunosuppressive responses in dendritic cells; however by functionalization, they can be engineered to provide controlled immune stimulation [7]. Consequently, CNTs are desirable for use in lung cancer immunotherapy if properly functionalized.

CONCLUSION AND FUTURE PERSPECTIVES

CNT-based nanovaccines represent a significant advancement in cancer immunotherapy, particularly for lung cancer. By efficiently establish connections between antigen-presenting cells and cytotoxic T-cells, CNTs bridge innate and adaptive immunity, promoting robust humoral and cellular immune responses against tumors. This targeted immunomodulatory strategy offers a promising therapeutic avenue for challenging cases, including metastatic and refractory lung cancer. To facilitate clinical translation, future research must systematically address key translational questions, including the long-term *in vivo* biodistribution, toxicity, optimal dosing, and immunogenicity profiles of CNT nanovaccines. Additionally, a deeper understanding of immune activation kinetics and potential autoimmune risks will be essential to ensure both efficacy and safety. With continued optimization, CNT-based nanovaccines hold considerable potential to reshape the therapeutic landscape of lung cancer immunotherapy.

ACKNOWLEDGEMENTS

None.

CONFLICT OF INTEREST

The authors declare they have no conflict of interests.

[DOI: 10.52547/vacres.10.2.56]

REFERENCES

1. Sheikhpour M, Maleki M, Sakhi H, Movafagh A, Nojoumi SA, Ghazizadeh L. Nano delivery of MiR-146a and its effect study on genes involved in apoptosis and autophagy pathways in lung cancer and tuberculosis. BMC Biotechnology. 2025;25(1):81. doi:10.1186/s12896-025-01019-8.
2. Sheikhpour M, Golbabaie A, Kasaeian A. Carbon nanotubes: A review of novel strategies for cancer diagnosis and treatment. Materials Science and Engineering: C. 2017;76(1):1289-304. doi:https://doi.org/10.1016/j.msec.2017.02.132.
3. Hassan HAFM, Smyth L, Wang JTW, Costa PM, Ratnasothy K, Diebold SS et al. Dual stimulation of antigen presenting cells using carbon nanotube-based vaccine delivery system for cancer immunotherapy. Biomaterials. 2016;104:310-22. doi:https://doi.org/10.1016/j.biomaterials.2016.07.005.
4. Hassan HAFM, Diebold SS, Smyth LA, Walters AA, Lombardi G, Al-Jamal KT. Application of carbon nanotubes in cancer vaccines: Achievements, challenges and chances. Journal of Controlled Release. 2019;297(10):79-90. doi:https://doi.org/10.1016/j.jconrel.2019.01.017.
5. Scheinberg DA, McDevitt MR, Dao T, Mulvey JJ, Feinberg E, Alidori S. Carbon nanotubes as vaccine scaffolds. Advanced Drug Delivery Reviews. 2013;65(15):2016-22. doi:https://doi.org/10.1016/j.addr.2013.07.013.
6. Rahimi E, Kariman A, Sheikhpour M. A Global Overview of Tuberculosis Vaccine Development. Vaccine Research. 2022;9(2):47-55. doi:10.61186/vacres.9.2.47.
7. Gottardi R, Douradinha B. Carbon nanotubes as a novel tool for vaccination against infectious diseases and cancer. Journal of Nanobiotechnology. 2013;11(1):30. doi:10.1186/1477-3155-11-30.
8. Hassan HAFM, Smyth L, Rubio N, Ratnasothy K, Wang JTW, Bansal SS et al. Carbon nanotubes' surface chemistry determines their potency as vaccine nanocarriers in vitro and in vivo. Journal of Controlled Release. 2016;225(10):205-16. doi:https://doi.org/10.1016/j.jconrel.2016.01.030.
9. Villa CH, Dao T, Ahearn I, Fehrenbacher N, Casey E, Rey DA et al. Single-Walled Carbon Nanotubes Deliver Peptide Antigen into Dendritic Cells and Enhance IgG Responses to Tumor-Associated Antigens. ACS Nano. 2011;5(7):5300-11. doi:10.1021/nn200182x.
10. Angaji SG, Salim MA, Azizi A, Amiri N, Rastakhiz S, Jahani N et al. The Power of Nanovaccines in Immunotherapy of Melanoma, Lung, Breast, and Colon Cancers: A Comprehensive Review. Research in Biotechnology and Environmental Science. 2023;2(4):55-64. doi:10.58803/rbes.v2i4.21.
11. Kreutz M, Giquel B, Hu Q, Abuknesha R, Uematsu S, Akira S et al. Antibody-antigen-adjuvant conjugates enable co-delivery of antigen and adjuvant to dendritic cells in cis but only have partial targeting specificity. PloS one. 2012;7(7):e40208. doi:10.1371/journal.pone.0040208.
12. Pescatori M, Bedognetti D, Venturelli E, Ménard-Moyon C, Bernardini C, Muresu E et al. Functionalized carbon nanotubes as immunomodulator systems. Biomaterials. 2013;34(18):4395-403. doi:https://doi.org/10.1016/j.biomaterials.2013.02.052.
13. Guo C, Al-Jamal WT, Toma FM, Bianco A, Prato M, Al-Jamal KT et al. Design of Cationic Multiwalled Carbon Nanotubes as Efficient siRNA Vectors for Lung Cancer Xenograft Eradication. Bioconjugate Chemistry. 2015;26(7):1370-9. doi:10.1021/acs.bioconjchem.5b00249.
14. Coccini T, Roda E, Sarigiannis DA, Mustarelli P, Quartarone E, Profumo A et al. Effects of water-soluble functionalized multi-walled carbon nanotubes examined by different cytotoxicity methods in human astrocyte D384 and lung A549 cells. Toxicology. 2010;269(1):41-53. doi:https://doi.org/10.1016/j.tox.2010.01.005.
15. Madkour L. Carbon Nanotubes-Based Intelligent Platform for Cancer Vaccine Co-delivery Nanocarriers Immunotherapy Achievements: Challenges In vitro and In vivo. International journal of nursing care and research. 2023;1:1-56.
16. Huang T, Liu L, Lv Z, Zhao K, Yi Q, Zhang J. Recent Advances in DNA Vaccines against Lung Cancer: A Mini Review. Vaccines (Basel). 2022;10(10):1586.
17. Alfei S, Reggio C, Zuccari G. Carbon Nanotubes as Excellent Adjuvants for Anticancer Therapeutics and Cancer Diagnosis: A Plethora of Laboratory Studies Versus Few Clinical Trials. cells. 2025;14(14):1052.
18. Mueller SN, Tian S, DeSimone JM. Rapid and Persistent Delivery of Antigen by Lymph Node Targeting PRINT Nanoparticle Vaccine Carrier To Promote Humoral Immunity. Molecular Pharmaceutics. 2015;12(5):1356-65. doi:10.1021/mp500589c.
19. de Carvalho Lima EN, Diaz RS, Justo JF, Castilho Piqueira JR. Advances and Perspectives in the Use of Carbon Nanotubes in Vaccine Development. International Journal of Nanomedicine. 2021;16(12):5411-35. doi:10.2147/IJN.S314308.
20. Huang Y, Zeng J. Recent development and applications of nanomaterials for cancer immunotherapy. Nanotechnology Reviews. 2020;9(1):367-84. doi:doi:10.1515/ntrev-2020-0027.
21. Dacoba TG, Olivera A, Torres D, Crecente-Campo J, Alonso MJ. Modulating the immune system through nanotechnology. Seminars in Immunology. 2017;34:78-102. doi:https://doi.org/10.1016/j.smim.2017.09.007.
22. Zhang Y, Lin S, Wang XY, Zhu G. Nanovaccines for cancer immunotherapy. Wiley interdisciplinary reviews Nanomedicine and nanobiotechnology. 2019;11(5):e1559. doi:10.1002/wnan.1559.
23. Li Y, Xu Z, Qi Z, Huang X, Li M, Liu S et al. Application of Carbon Nanomaterials to Enhancing Tumor Immunotherapy: Current Advances and Prospects. International Journal of Nanomedicine. 2024;19(26):10899-915. doi:10.2147/IJN.S480799.
24. Liu N, Xiao X, Zhang Z, Mao C, Wan M, Shen J. Advances in Cancer Vaccine Research. ACS Biomaterials Science & Engineering. 2023;9(11):5999-6023. doi:10.1021/acsbiomaterials.3c01154.
25. Dong J, Ma Q. Myofibroblasts and lung fibrosis induced by carbon nanotube exposure. Particle and fibre toxicology. 2016;13(1):60. doi:10.1186/s12989-016-0172-2.
26. Kagan VE, Konduru NV, Feng W, Allen BL, Conroy J, Volkov Y et al. Carbon nanotubes degraded by neutrophil myeloperoxidase induce less pulmonary inflammation. Nature nanotechnology. 2010;5(5):354-9. doi:10.1038/nnano.2010.44.
27. Liu Y, Zhao Y, Sun B, Chen C. Understanding the toxicity of carbon nanotubes. Accounts of chemical research. 2013;46(3):702-13. doi:10.1021/ar300028m.
28. Shvedova AA, Pietroiusti A, Fadeel B, Kagan VE. Mechanisms of carbon nanotube-induced toxicity: focus on oxidative stress. Toxicology and applied pharmacology. 2012;261(2):121-33. doi:10.1016/j.taap.2012.03.023.
29. Tkach AV, Shurin GV, Shurin MR, Kisin ER, Murray AR, Young SH et al. Direct effects of carbon nanotubes on dendritic cells induce immune suppression upon pulmonary exposure. ACS Nano. 2011;5(7):5755-62. doi:10.1021/nn2014479.

[DOI: 10.52547/vacres.10.2.56]