South Russian Journal of Cancer. 2025. Vol. 6, No. 3. P. 63-76
https://doi.org/10.37748/2686-9039-2025-6-3-7
https://elibrary.ru/oxfxgi
REVIEW

Lymph nodes as a target for the use of dendritic cell vaccines: modern approaches and prospects

E. M. Frantsiyants, V. A. Bandovkin✉, T. I. Moiseenko, Yu. A. Petrova, I. A. Goroshinskaya, G. V. Zhukova, L. K. Trepitaki, E. I. Surikova

National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation
✉ valerryana@yandex.ru

ABSTRACT

This article provides an overview of current approaches to cancer immunotherapy, with an emphasis on the role of dendritic cells (DCs), lymph nodes (LNs), and innovative methods of vaccine delivery. Immunotherapy using DC-based vaccines represents a promising direction, capable of stimulating a specific immune response against tumor cells and forming long-term immune memory. Tumor-draining lymph nodes (TDLNs) play a key role in immune activation, as they are the sites where dendritic cells present tumor antigens and activate T-cells. In cancer, unlike viral infections, CD8+ T-cell activation occurs in two stages, and the effectiveness of this process depends on signals from the tumor microenvironment, which explains why the immune response to cancer is often weak.

The article also discusses modern strategies for delivering vaccines to lymph nodes, including the use of nanoparticles, bioorthogonal reactions, and photothermally induced materials. These approaches help overcome the "granularity paradox", associated with the need to balance vaccine size for LN penetration and uptake by immune cells. The prospects of adoptive cell therapy using T-cells from TDLNs, as well as the role of exosomes and whole-cell tumor antigens in the development of effective vaccines, are also considered. Combination strategies, such as the use of vaccines together with checkpoint inhibitors (e.g., anti-PD1), demonstrate potential for enhancing antitumor immunity.

The further advancement of cancer immunotherapy requires the integration of new knowledge about the biology of dendritic cells, modern methods of cell engineering, and nanotechnology to create personalized and effective antitumor vaccines.

Keywords: cancer, dendritic cells, lymph nodes, dendritic cell vaccine, nano vaccines, exosomes, neoantigens, personalized medicine

For citation: Frantsiyants E. M., Bandovkina V. A., Moiseenko T. I., Petrova Yu. A., Goroshinskaya I. A., Zhukova G. V., Trepitaki L. K., Surikova E. I. Lymph nodes as a target for the use of dendritic cell vaccines: modern approaches and prospects. South Russian Journal of Cancer. 2025; 6(3): 63-76. https://doi.org/10.37748/2686-9039-2025-6-3-7, https://elibrary.ru/oxfxgi

For correspondence: Valeriya A. Bandovkina – Dr. Sci. (Biol.), senior researcher at the Laboratory for the Study of Pathogenesis of Malignant Tumors, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation
Address: 63 14 line str., Rostov-on-Don 344037, Russian Federation
E-mail: valerryana@yandex.ru
ORCID: https://orcid.org/0000-0002-2302-8271
SPIN: 8806-2641, AuthorID: 696989
ResearcherID: AAG-8708-2019
Scopus Author ID: 57194276288

Funding: this work was not funded

Conflict of interest: the authors declare that there are no obvious and potential conflicts of interest associated with the publication of this article

The article was submitted 04.04.2025; approved after reviewing 31.07.2025; accepted for publication 14.08.2025

Южно-Российский онкологический журнал. 2025. Т. 6, № 3. С. 63-76
https://doi.org/10.37748/2686-9039-2025-6-3-7
https://elibrary.ru/oxfxgi
3.1.6. Онкология, лучевая терапия

ОБЗОР

Лимфатические узлы как точка приложения при использовании дендритноклеточных вакцин: современные стратегии усиления иммунного ответа

Е. М. Франциянц, В. А. Бандовкина✉, Т. И. Моисеенко, Ю. А. Петрова, И. А. Горошинская, Г. В. Жукова, Л. К. Трепитаки, Е. И. Сурикова

ФГБУ «Национальный медицинский исследовательский центр онкологии» Министерства здравоохранения Российской Федерации, г. Ростов-на-Дону, Российская Федерация
✉ valerryana@yandex.ru

РЕЗЮМЕ

Статья представляет собой обзор современных подходов к иммунотерапии рака, акцентируя внимание на роли дендритных клеток (ДК), лимфатических узлов (ЛУ) и инновационных методов доставки вакцин. Иммунотерапия с применением вакцин на основе ДК представляет собой перспективное направление, способное стимулировать специфический иммунный ответ против опухолевых клеток и формировать долговременную иммунную память. Дренирующие опухоль лимфатические узлы (TDLN) играют ключевую роль в активации иммунного ответа, так как именно в них происходит презентация опухолевых антигенов дендритными клетками и активация Т-клеток. При раке, в отличие от вирусных инфекций, активация CD8+ Т-клеток происходит в два этапа, и эффективность процесса зависит от сигналов, поступающих из опухолевого микроокружения, что объясняет, почему иммунный ответ на рак часто бывает слабым.
В статье также обсуждаются современные стратегии доставки вакцин в лимфатические узлы, включая использование наночастиц, биоортогональных реакций и фототермически индуцированных материалов. Эти подходы позволяют преодолеть «парадокс гранулярности», связанный с необходимостью баланса между размером вакцин для их проникновения в ЛУ и захвата иммунными клетками.
Рассматриваются перспективы адаптивной клеточной терапии с использованием Т-клеток из TDLN, а также роль экзосом и цельноклеточных опухолевых антигенов в создании эффективных вакцин. Комбинированные подходы, такие как сочетание вакцин с ингибиторами контрольных точек (например, анти-PD1), демонстрируют потенциал для усиления противоопухолевого иммунитета.
Дальнейшее развитие иммунотерапии рака требует интеграции новых знаний о биологии дендритных клеток, современных методов клеточной инженерии и нанотехнологий для создания персонализированных и эффективных противоопухолевых вакцин.

Ключевые слова: рак, дендритные клетки, лимфатические узлы, дендритноклеточная вакцина, нановакцины, экзосомы, неоантигены, персонализированная медицина

Для цитирования: Франциянц Е. М., Бандовкина В. А., Моисеенко Т. И., Петрова Ю. А., Горошинская И. А., Жукова Г. В, Трепитаки Л. К., Сурикова Е. И. Лимфатические узлы как точка приложения при использовании дендритноклеточных вакцин: современные стратегии усиления иммунного ответа. Южно-Российский онкологический журнал. 2025; 6(3): 63-76. https://doi.org/10.37748/2686-9039-2025-6-3-7, https://elibrary.ru/oxfxgi

Для корреспонденции: Бандовкина Валерия Ахтямовна – д.б.н., ведущий научный сотрудник лаборатории изучения патогенеза злокачественных опухолей, ФГБУ «Национальный медицинский исследовательский центр онкологии» Министерства здравоохранения Российской Федерации, г. Ростов-на-Дону, Российская Федерация
Адрес: 344037, Российская Федерация, г. Ростов-на-Дону, ул. 14-я линия, д. 63
E-mail: valerryana@yandex.ru
ORCID: https://orcid.org/0000-0002-2302-8271
SPIN: 8806-2641, AuthorID: 696989
ResearcherID: AAG-8708-2019
Scopus Author ID: 57194276288

Финансирование: финансирование данной работы не проводилось

Конфликт интересов: все авторы заявляют об отсутствии явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи

Статья поступила в редакцию 04.04.2025; одобрена после рецензирования 31.07.2025; принята к публикации 14.08.2025

BACKGROUND

In recent years, cancer immunotherapy has revolutionized the traditional paradigm of cancer treatment [1]. Interest in tumor vaccines has been growing due to their ability to elicit specific immune responses and to establish durable immune memory [2]. This progress has opened new opportunities for the development of more effective cancer treatment strategies, including the use of dendritic cells (DCs) in immunotherapy.

Immunotherapy using DC-based vaccines represents a biologically rational approach that harnesses the patient's immune system to eliminate malignant cells. The development of DC-based technologies has become possible owing to the study of impaired differentiation and functional alterations of DCs in cancer [3]. DCs, which play a pivotal role in T-cell activation, constitute the foundation of modern immunotherapy strategies aimed at restoring the functional activity of exhausted T cells within the tumor microenvironment [4]. These advances have led to a significant increase in the number of clinical trials of DC-based vaccines over the past three decades. Most of these vaccines are autologous and derived from patient monocytes; however, in recent years, the spectrum of DC subtypes utilized has expanded.

As a rule, tumor antigens are introduced into patient-derived DCs *ex vivo* prior to adjuvant therapy. With the advent of personalized medicine, tumor neoantigens are increasingly being employed to develop individually tailored vaccines. Therapeutic cancer vaccines based on cells utilize different sources of antigens, including autologous tumor cells obtained from the patient, allogeneic cancer cell lines, and autologous antigen-presenting cells (APCs). These vaccines mimic natural immune processes by stimulating an adaptive immune response against tumor antigens [5]. However, for successful immune activation, it is critical to understand the role of lymph nodes (LNs) in this process, as they are strategically positioned immune organs where antigens drain from peripheral tissues.

Purpose of the study: to summarize current advances in the development of cancer immunotherapy strategies, with a particular focus on the role of dendritic cells and lymph nodes in shaping the antitumor immune response.

The Role of Lymph Nodes in the Formation of the Immune Response

LNs harbor various immune cells, including APCs, B lymphocytes, T lymphocytes, and natural killer cells. They are key organs for immune surveillance, regulation, and APC activation [6]. DCs, with their ability to cross-present antigens, play a particularly important role in this process. LNs contain a significant population of phagocytic DCs, well known for their cross-presentation capacity [7]. This refers to the presentation of exogenous antigens to CD8+ T cells via major histocompatibility complex class I (MHC I), which results in the production of cytotoxic T lymphocytes that specifically destroy tumor cells [8]. An increasing body of evidence supports that tumor vaccines targeted to LNs significantly enhance immune responses [9–12].

Tumor-draining lymph nodes (TDLNs) are the first LNs reached by tumor cells through lymphatic vessels. Within TDLNs, DCs capture and present tumor antigens, activating T cells in the paracortical zone of the LN. In other words, TDLNs serve as immune compartments where antitumor immune responses are generated and regulated [13]. This makes TDLNs a critical element in the development of new immunotherapy strategies.

The Two-Step Model of CD8+ T-Cell Activation in Malignancies

Studies by Prokhnevska N, et al. [14] demonstrated that CD8+ T cells, which typically combat infections and tumors, are activated and function differently in neoplasia compared with viral infections. In response to malignant tumors, CD8+ T-cell activation occurs in two stages:

Initial priming: In TDLNs, CD8+ T cells acquire a "stem-like phenotype". This means they remain in an immature state, retaining the capacity for long-term persistence and proliferation. Upon encountering tumor antigens, CD8+ T cells begin proliferating within the TDLN. However, unlike their response to viruses, they do not immediately differentiate into mature effector cells. Instead, they preserve their "stem-like phenotype", which allows them to remain immature for years in human LNs.

Co-stimulatory phase: These immature T cells gradually migrate from the LN into the tumor. Once there, they receive additional signals that trigger

changes in gene activity (transcriptional and epigenetic reprogramming), enabling them to become fully competent "killers" of tumor cells. A range of activating co-stimulatory receptors expressed on CD8+ T cells play a crucial role in shaping T-cell function, such as CD28, NKG2D, 4-1BB, and OX-40. These receptors transmit signals that enhance T-cell responses, ultimately supporting T-cell proliferation and survival, cytokine production, and the generation and maintenance of memory T cells, despite initial activation through distinct signaling pathways. Each receptor appears to induce these functions to varying degrees, and this differential signaling alters gene expression profiles and effector functions, creating a unique activation state [15].

The two-step model of T-cell activation helps explain why anti-PD1 checkpoint blockade therapy does not work for all patients. Tcf1+ CD8+ T cells, which expand in response to anti-PD1, require a CD28 co-stimulatory signal for successful activation [16–18].

CD8+ T cells play a central role in the adaptive immune response to neoplasia. Their abundance and activity within the tumor can serve as important prognostic factors: the higher the infiltration of such cells, the greater the likelihood of patient survival and favorable response to therapy, including checkpoint inhibitors [19, 20].

Table 1. Classification of Current Approaches in Cancer Immunotherapy

Category	Approach		Example	Advantages	Limitations
Antigen modification	Chemical conjugation	Conjugation of antigens with lipids/ polymers to improve delivery	DSPE-OVA-Gel (Zhou L, et al.)	Enhanced lymph node drainage, precise delivery	Standardization challenges
	Nanotechnology-based platforms	Use of nanoparticles for controlled delivery	Phase-transition vaccines (Wang J, et al.), DNA nanoparticles (Zha Y, et al.)	Dynamic size control, enhanced immune response	Potential toxicity, manufacturing complexity
	Alternative antigen sources	Use of whole-cell vaccines, exosomes, iPSCs	α-melittin-NP (Yu X, et al.), Hy-M-Exo (Xu J, et al.)	Broad antigen spectrum, personalization	Tumor heterogeneity, limited efficacy
Нагрузка ДК	*Ex vivo*	Loading dendritic cells with antigens prior to reinfusion	DCvax-IT (Sprooten J, et al.)	Personalized approach, T-cell activation	Labor-intensive, high cost
	In vivo	Targeting dendritic cells in situ (hydrogels, bioorthogonal chemistry)	DSPE-OVA-Gel (Zhou L, et al.), bioorthogonal modification (Qin H, et al.)	Simplified delivery, minimized side effects	Limited efficacy in certain tumor types
Combination therapy	ACT + vaccines	Use of T cells from TDLN or neoantigen-specific T cells	ACT (Okamura K, et al.), OCDC (Li Q, et al.)	Enhanced immune response, overcoming immunosuppression	Low frequency of neoantigen-specific T cells
	Checkpoint inhibitors	Combination with PD-L1/PD-1 blockers	DCvax-IT + anti-PD-L1 (Sprooten J, et al.)	Strengthened antitumor response, overcoming resistance	Side effects, high cost

The tumor microenvironment also plays a critical role in this process. In the absence of specific signals, T cells cannot become effective effectors, which explains why antitumor immune responses are often weak. Importantly, the signals necessary for T cells to become cytotoxic do not occur during the initial priming stage (as in viral infections) but are generated only after T cells migrate into the tumor [14]. This finding emphasizes that the tumor microenvironment is essential for T-cell activation and that its dysfunction renders antitumor immunity ineffective.

Thus, antitumor immune activity is primarily induced in TDLNs, which play a key role in shaping effective antitumor T-cell responses [13, 21, 22]. To date, a wide range of immunotherapeutic approaches for malignant tumors has been developed, summarized in Table 1.

Utilization of Lymph Nodes in Immunotherapy

Currently, the development of cancer immunotherapy with antitumor vaccines is progressing in two directions: the generation of cytotoxic T lymphocyte (CTL) populations *ex vivo* (adoptive cell therapy) and *in vivo* through natural immunological mechanisms occurring within lymph nodes (LNs).

During surgical procedures, tumor-draining lymph nodes (TDLNs) are usually removed together with the primary tumor(s) to eliminate potential residual tumor cells, and the excised LNs are examined for metastatic involvement [23]. It is now well established that extensive LN dissection has provided little clinical benefit in terms of long-term survival for patients with colorectal cancer (CRC) with high microsatellite instability/deficient mismatch repair [24]. It is assumed that preservation of LNs may be beneficial for host immune responses against tumor cells [25]. An interesting study by Okamura K, et al. [26] investigated the potential of non-metastatic LNs as a novel therapeutic option for CRC patients with poor prognosis. The authors questioned whether TDLN removal deprives the body of an important antitumor resource and explored the possibility of using these LNs to improve immunotherapy outcomes in CRC. Okamura K, et al. [26] proposed employing LNs for adoptive cell therapy a method in which T cells are isolated from patient LNs, expanded *ex vivo*, and subsequently reintroduced into the body to exert antitumor effects. Their results demonstrated that non-metastatic LNs could serve as a viable source of cells for this therapeutic strategy.

Adoptive cell therapy using neoantigen-specific T cells represents a promising immunotherapeutic approach. However, the naturally low frequency of these cells in patients makes their detection and screening a challenging task, limiting broad clinical application. To overcome these obstacles, Li Q, et al. [27] proposed a strategy for preparing neoantigen-specific T cells for adjuvant therapy following immunization with dendritic cell (DC) vaccines loaded with oxidized tumor cell lysates (OCDC). Theoretically, this strategy offers several advantages and clinical potential. First, preventive administration of the OCDC vaccine improves the condition of immunosuppressed patients, induces neoantigen-specific immune responses, and facilitates the preparation of neoantigen-reactive T cells by eliminating the need for labor-intensive screening. Second, OCDC vaccine preparation is simple and rapid, and pre-vaccination enables timely initiation of patient treatment, thereby increasing the likelihood of therapeutic success. Moreover, combining OCDC vaccination with neoantigen-reactive T cells enhances efficacy in patients with non-small cell lung cancer, CRC, and melanoma, and this approach could potentially be extended to other immunogenic tumors.

The development of the second direction *in vivo* generation of CTL populations requires novel vaccine delivery strategies aimed at enhancing the immune response.

Modern Strategies for Vaccine Delivery

Given their key role in antitumor immunity, lymph nodes (LNs) are considered a primary target for cancer immunotherapy. Targeted delivery of antigens and adjuvants to LNs enables modulation of their microenvironment, thereby enhancing immune responses, and represents a promising avenue in anticancer vaccine development. Many researchers believe that efficient and precise delivery of tumor vaccines to LNs where they are taken up by antigen-presenting cells (APCs) is a critical determinant for achieving effective antigen presentation and subsequent induction of potent antitumor vaccine effects [6, 10, 28].

A major challenge in this context is the design of vaccine particle size optimized for LN target-

ing. The so-called "granularity paradox" regarding LN delivery and subsequent APC uptake remains a critical issue in the development of effective cancer vaccines. On the one hand, a particle size of 10–100 nm is favorable for lymphatic drainage. Larger particles tend to be trapped in the interstitial matrix, whereas smaller ones are more likely to enter systemic circulation. On the other hand, particles ranging from 50–500 nm are most efficiently internalized by dendritic cells (DCs), with larger sizes stimulating more robust uptake and activation. Thus, an optimal balance is required vaccines must be designed with dimensions that ensure both enhanced lymphatic drainage and efficient DC uptake [6, 29].

To address this issue, Wang J, et al. [29] developed a phase-transition vaccine with dynamically modulated particle size, based on a thermosensitive polymer conjugated with a photothermally responsive molecule and an antigen. Initially small in size (~20 nm), the vaccine drained efficiently into LNs and then transformed *in situ* into larger particles (~480 nm) upon exposure to an external trigger (laser irradiation). This size modulation promoted efficient LN DC endocytosis, ultimately leading to a rapid and robust *in vivo* antitumor response [29].

A different approach was demonstrated by Zha Y, et al. [6], who designed a novel tumor vaccine based on manganese dioxide (MnO_2) nanoparticles for LN delivery. These nanoparticles exhibited an optimal size (~90 nm), facilitating LN penetration. To enhance immune cell uptake, the nanoparticles were coated with short DNA chains, which increased their size. This DNA base-pairing strategy for controlling nanoparticle size, thereby improving antigen presentation and vaccine efficacy, represents a new concept for anticancer vaccine development. Importantly, vaccines must not only reach LNs but also be rapidly internalized by APCs. Otherwise, they may pass through the subcapsular sinus into peripheral LN regions and exit via efferent lymphatic vessels [30]. Nanovaccines meeting both criteria efficient LN drainage and APC endocytosis hold significant promise.

In addition to particle size optimization, Qin H, et al. [31] proposed direct LN targeting via chemical modification of lymphatic endothelial cell surfaces (bioorthogonal reaction). Their results demonstrated improved delivery of encapsulated antigens and adjuvants into LNs, leading to a stronger *in vivo* CD8+ T-cell response. This strategy resulted in markedly enhanced therapeutic efficacy, including

Table 2. Comparison of vaccine delivery strategies to lymph nodes

Strategy	Particle Size	Mechanism of Action	Efficacy	Clinical Potential
Phase-transition vaccines	20–480 nm	Dynamic size alteration under external stimuli (laser)	High, enhanced dendritic cell endocytosis	Flexibility, controllable activation
DNA-functionalized nanoparticles	~90 nm	Size control through DNA base-pairing	High, optimal balance of drainage and uptake	ersonalization, low toxicity
Hybrid nanovesicles (Hy-M-Exo)	30–150 nm	Combination of tumor-derived exosomes and dendritic cell membranes	Very high, T-cell activation and Treg suppression	Multifunctionality
Bioorthogonal modificatio	–	Chemical alteration of lymphatic vessels to improve delivery	Moderate, tumor-type dependent	Broad spectrum of applications

prolonged survival in mice with metastatic melanoma [31].

A summary of the approaches discussed in this section is provided in Table 2.

Nanovaccines

Several recent studies have shown that the delivery of nanovaccines to lymph nodes (LNs) activates both humoral and cellular immune responses to combat neoplasia [32]. Somatic mutations generate specific neoantigens – unique tumor antigens that play a crucial role in antitumor immune responses [33, 34]. However, the number of available tumor-associated antigens (TAAs) necessary for vaccine development is limited for most tumor types [35], and the prediction and identification of individual tumor-associated neoantigens remain challenging due to the complexity of the required technologies [33, 36]. To overcome the lack of knowledge about specific tumor antigens and to ensure accurate delivery to LNs, various approaches have been explored.

Adaptive immune responses rely on the ability of mature dendritic cells (DCs) to migrate to LNs for further antigen presentation. Considering this, Zhou L, et al. [37] developed a DSPE-ovalbumin (DSPE-OVA) peptide using one-step chemical crosslinking of DSPE-PEG and the model antigen peptide OVA. This peptide accumulates in lymphoid organs through interaction with endogenously migrated DCs. To enhance antigen uptake, the authors created an injectable DSPE-OVA hydrogel (DSPE-OVA-Gel), which serves as a local environment for vaccine transport via DCs. The hydrogel is composed of pH-sensitive DSPE-OVA, granulocyte-macrophage colony-stimulating factor (GM-CSF) to recruit and activate DCs, and porous PLGA (polylactide-co-glycolide) microspheres that facilitate cell attachment. Upon recruitment, the DSPE-OVA hydrogel efficiently integrates into DC membranes due to the high affinity of the lipophilic DSPE tail for cell membranes, thereby enhancing antigen uptake. This process ensured a high concentration of OVA without damaging the membrane or disrupting DC signal transmission. Owing to the natural ability of mature DCs to migrate to LNs, OVA-loaded cells effectively reached their target. In the acidic LN microenvironment, OVA was released from the cell surface and delivered to local APCs. This study demonstrates that an injectable combined hydrogel vaccine significantly enhances antitumor immunity by ensuring precise antigen delivery to LNs and stimulating a robust adaptive immune response.

To address the weak immunoreactivity of LNs caused by inefficient stimulation of cytotoxic T lymphocytes, Liu M, et al. [38] developed a nanovaccine mimicking high-density lipoproteins (HDLs), loaded with the chemotherapeutic drug docetaxel. This platform represents a system for delivering chemotherapy into the tumor microenvironment (glioblastoma). The results showed that dying tumor cells released tumor antigens, which were subsequently captured *in situ* by DCs, initiating the activation of antigen-specific CD8+ T cells that directly induced tumor cell death. The authors examined the efficiency of LN delivery and DC uptake of the nanoparticles using fluorescence imaging and flow cytometry. The optimized nanovaccine facilitated simultaneous delivery of antigens and adjuvants to LNs and sustained antigen presentation by DCs, which resulted in a long-term immune response characterized by increased cytotoxic lymphocyte frequency in lymphoid organs and tumor tissue. Immunization with the nanovaccine significantly suppressed tumor formation and growth and enhanced the therapeutic efficacy of immune checkpoint inhibitors, particularly in highly malignant melanoma models in mice.

Compared with vaccines based on specific tumor antigens, whole-cell tumor vaccines contain a broad spectrum of antigens, thereby avoiding the costly and labor-intensive process of TAA (neoantigen) identification for a specific tumor type. Importantly, whole-cell tumor vaccines have the potential to elicit a stronger antitumor immune response, markedly reducing the likelihood of tumor development and recurrence. Based on this concept, Yu X, et al. [36] hypothesized that the ideal LN-targeted nanovaccine should employ the full spectrum of tumor antigens rather than individual neoantigens or model antigens. This approach would enable a sustained immune response against multiple tumor antigen epitopes by activating both CD4+ and CD8+ tumor-specific T cells. The authors discovered that α-melittin-NP, a peptide-phospholipid scaffold mimicking

high-density lipoproteins (HDLs), could serve as an effective nanovaccine even without specific tumor antigens or adjuvants. On the one hand, α-melittin-NP retained the cytotoxic effect of melittin, inducing tumor antigen release at the injection site. On the other hand, α-melittin-NP of optimal size could efficiently penetrate LNs and acti vate local APCs. In experiments using a bilateral B16F10 melanoma mouse model, administration of α-melittin-NPs as a whole-cell nanovaccine induced a systemic immune response, resulting in suppression of primary tumor growth and even complete regression of distant tumors [36].

Use of Tumor Cell Lysates as a Source of Antigens

In several studies, tumor cell lysates, which contain fragments of tumor cells released during chemotherapy and irradiation, have been used as TAAs [39, 40]. However, tumor cell lysates with low immunogenicity may induce immune tolerance and reduce the efficiency of antigen uptake [41]. Moreover, the types and quantities of antigens released as a result of chemotherapy and irradiation vary among patients, making standardization of this approach difficult. Therefore, there is a need for novel strategies for vaccine development that are not dependent on specific TAAs.

Exosomes as an Alternative Source of Antigens

In recent years, exosomes membrane vesicles measuring 30–150 nm secreted by cells into the extracellular environment and involved in intercellular communication have gained increasing importance in the development of antitumor vaccines.

Tumor-derived exosomes have been found to contain multiple TAAs and neoantigens and effectively deliver them to DCs, thereby stimulating tumor-specific immunity [42]. Importantly, tumor exosomes demonstrated superior antitumor efficacy compared with tumor lysates as a source of antigens [43]. In this study, exosome-pulsed DCs induced significant inhibition of hepatocellular carcinoma (HCC) growth and a stronger immune response characterized by higher T lymphocyte counts, increased interferon-γ levels, and reduced interleukin-10 and transforming growth factor-β levels within tumor tissues in both ectopic and orthotopic murine models of HCC, compared with DCs pulsed with tumor lysates. Furthermore, the use of tumor-derived exosomes not only mediated specific cytolysis of HCC cells but also elicited cross-protective effects against pancreatic cancer cells [43]. Thus, this combined approach leveraging a complex array of tumor antigens with efficient targeted delivery to LNs, where APCs (DCs) and effector T cells interact renders tumor-derived exosomes a highly promising tool for the development of effective antitumor vaccines.

Hybrid Nanovesicles (Hy-M-Exo)

Building upon this concept, Xu J, et al. [44] developed hybrid nanovesicles (Hy-M-Exo), created by fusing tumor-derived exosomes with DC-derived membrane vesicles and incorporating monophosphoryl lipid A. The resulting Hy-M-Exo contained proteins characteristic of DCs, such as CD86 (an activation marker) and CCR7 (a receptor responsible for LN homing), and showed significant effects within the paracortical LN region, where DCs and T cells are located. Hy-M-Exo induced robust DC activation and stimulated T-cell immune responses in LNs, leading to strong inhibition of head and neck squamous cell carcinoma growth in mice. Additionally, the authors found that Hy-M-Exo could suppress immunosuppressive regulatory T cells, further enhancing the immune response. These findings highlight the potential of hybrid nanovesicles to amplify immune responses and inhibit tumor growth. The authors also proposed that delivering antitumor agents into LNs via the CCR7-CCL21/19 pathway (a mechanism regulating LN homing) represents a promising strategy [44].

Dendritic Cell-Based Vaccines

In parallel, immune surveillance of poorly immunogenic tumors can be enhanced through dendritic cell (DC)-based vaccines designed to stimulate antigen-specific immune responses, for example, by using targeted therapies directed at myeloid cells. Myeloid cells (including monocytes, macrophages, and DCs) are key components of the tumor microenvironment (TME), performing diverse functions ranging from immunosuppressive to immunostimulatory. The myeloid cell pool is highly heterogeneous comprising monocytes, macrophages, DCs, and granulocytes and exhibits remarkable plasticity, with the capacity to differentiate into dif-

ferent phenotypes depending on TME signals [45]. Perez CR and De Palma M [46], investigating the role of DC subtypes in the TME, placed particular emphasis on conventional type 1 DCs. These cells are able to migrate between lymphoid and non-lymphoid tissues, thereby regulating cytokine and chemokine distribution, which influences both inflammation and lymphocyte trafficking. DCs are considered uniquely capable of cross-presentation, i. e., presenting exogenous antigens to CD8+ T cells in lymph nodes [47].

Despite their immunogenic potential, DC-based vaccines have not yet achieved widespread clinical application due to difficulties in standardization and limited efficacy in some patients. In this context, Sprooten J, et al. [48] found that the major limitation of human DC-based vaccines is the diversity of their functional states rather than the process of maturation. The authors identified the most immunogenic DC vaccine state, which correlated with effective antigen-specific immunity and favorable clinical responses in patients with various tumors. Surprisingly, their preclinical vaccine DCvax-IT performed suboptimally: instead of promoting effector T-cell formation, it increased the number of PD-L1$^+$ lymphoid-associated macrophages (LAMs) via activation of the type I interferon pathway and associated genes. Moreover, DCvax-IT stimulated pre-existing tumor-associated macrophages (TAMs) expressing PD-L1, thereby suppressing T-cell activity and creating an immunosuppressive environment. This mechanism was identified as a key factor underlying resistance to DCvax-IT. Importantly, combining DCvax-IT with PD-L1 inhibitors successfully controlled tumors in immunodeficient mice phenotypic analogues of human tumors with T-cell deficiency [48]. These findings demonstrate the potential to enhance the efficacy of immunological interventions in human tumors with impaired effector cell function.

Induced Pluripotent Stem Cells (iPSCs)

In addition to tumor lysates and tumor-derived exosomes, induced pluripotent stem cells (iPSCs) are also being explored as a promising source of tumor antigens. iPSCs express a broad spectrum of tumor-associated antigens and can induce immune responses that prevent the development of various tumor types. However, iPSCs face certain limitations, including potential oncogenicity, difficulties in delivery to lymph nodes and the spleen, and limited efficacy in suppressing tumor growth. Wang R, et al. [49] evaluated the antitumor effects of exosomes derived from iPSCs and incubated with DCs (DC+EXO) in murine melanoma models. The immune responses induced by the DC+EXO vaccine were assessed both *in vitro* and *in vivo* by analyzing T-cell activation and cytokine

Table 3. Alternative sources of tumor antigens

Source	Description	Advantages	Limitations
Tumor cell lysates	Cell fragments after chemotherapy/ irradiation	Broad spectrum of antigens	Low immunogenicity, variability among patients
Exosomes	Membrane vesicles (30–150 nm) carrying tumor antigens	Natural carriers, high biocompatibility	Isolation and standardization challenges
iPSCs	Induced pluripotent stem cells	Broad spectrum of antigens, potential for personalized therapy	Potential oncogenicity, difficulties in delivery
Hybrid nanovesicles (Hy-M-Exo)	Combination of tumor-derived exosomes and DC membranes	High immunogenicity, suppression of regulatory T cells (Treg)	Complex manufacturing process

levels. After DC+EXO vaccination, T cells isolated from the spleen exhibited high *in vitro* cytotoxicity against melanoma, lung cancer, breast cancer, and colorectal cancer cell lines. Moreover, DC+EXO vaccination induced long-term T-cell responses and prevented melanoma recurrence, while significantly suppressing primary melanoma growth and reducing lung metastases. Finally, biocompatibility studies confirmed that DC+EXO vaccination did not cause significant toxicity to normal cells or tissues in mice.

As shown above, multiple sources of tumor antigens are currently being investigated for the development of antitumor vaccines, each with specific advantages and limitations (Table 3).

Platforms for cell therapy

A promising avenue to increase the efficacy of tumor vaccines is the use of alternative mechanisms of antitumor cytotoxicity that do not rely exclusively on CD8+ T-cell activity. Ghasemi A, et al. [50] described a cell therapy platform based on mouse or human dendritic cell progenitors (DCPs), genetically engineered to express two immunostimulatory cytokines IL-12 and FLT3L. These modified DCPs differentiated into type 1 conventional DCs (cDC1s) and were able to suppress tumor growth, including melanoma and spontaneously arising liver tumors in mice, without prior antigen loading or myeloablative conditioning. The antitumor response resulted from synergy between IL-12 and FLT3L and was associated with infiltration and activation of natural killer (NK) cells and T cells, polarization of macrophages toward an M1 phenotype, and induction of ischemic necrosis in tumors. Importantly, the immunity induced was dependent on endogenous expansion of cDC1s and interferon-γ signaling, but not on CD8+ T-cell cytotoxicity. Moreover, cytokine-expressing DCPs interacted effectively with GD2-targeted CAR-T cells, enhancing their proliferation and cytotoxicity against intracranial gliomas in mice, highlighting the potential of combining DCPs with adoptive cell therapy.

CONCLUSION

It is now clear that lymph nodes (LNs) not only maintain immune homeostasis but also act as central hubs for dendritic cell-mediated antitumor immunity. Recognizing LNs as therapeutic targets has enabled modern immunotherapy to advance toward the development of innovative dendritic cell vaccines (DCVs). Current strategies aim to improve precision of vaccine delivery into LNs, either by modulating particle size or by modifying lymphatic vessels, and to diversify sources of tumor antigens for dendritic cell presentation. The integration of tumor cell lysates, exosomes, hybrid nanovesicles, dendritic cell-based vaccines, induced pluripotent stem cells, and cell therapy platforms provides new opportunities to strengthen immune responses, minimize side effects, and enhance personalization. Combination approaches, including checkpoint blockade, offer a way to control tumors with effector-cell deficiencies and to overcome resistance of poorly immunogenic cancers. Despite the progress, challenges remain potential toxicity, selection of the most effective tumor antigens, antigen delivery, standardization of personalized vaccines, and large-scale production. Nevertheless, the diversification of dendritic cell-based vaccine strategies is expected to enable effective immunotherapy across the wide heterogeneity of malignancies and clinical contexts.

References

1. Yan S, Luo Z, Li Z, Wang Y, Tao J, Gong C, et al. Improving Cancer Immunotherapy Outcomes Using Biomaterials. Angew Chem Int Ed Engl. 2020 Sep 28;59(40):17332–17343. https://doi.org/10.1002/anie.202002780
2. Liu J, Liew SS, Wang J, Pu K. Bioinspired and Biomimetic Delivery Platforms for Cancer Vaccines. Adv Mater. 2022 Jan;34(1):e2103790. https://doi.org/10.1002/adma.202103790
3. Kurilin V, Alshevskaya A, Sennikov S. Development of Cell Technologies Based on Dendritic Cells for Immunotherapy of Oncological Diseases. Biomedicines. 2024 Mar 21;12(3):699. https://doi.org/10.3390/biomedicines12030699
4. Cabeza-Cabrerizo M, Cardoso A, Minutti CM, Pereira da Costa M, Reis e Sousa C. Dendritic Cells Revisited. Annu Rev Immunol. 2021 Apr 26;39:131–166. https://doi.org/10.1146/annurev-immunol-061020-053707

5. Tiwari A, Alcover K, Carpenter E, Thomas K, Krum J, Nissen A, et al. Utility of cell-based vaccines as cancer therapy: Systematic review and meta-analysis. Hum Vaccin Immunother. 2024 Dec 31;20(1):2323256. https://doi.org/10.1080/21645515.2024.2323256
6. Zha Y, Fu L, Liu Z, Lin J, Huang L. Construction of lymph nodes-targeting tumor vaccines by using the principle of DNA base complementary pairing to enhance anti-tumor cellular immune response. J Nanobiotechnology. 2024 May 8;22(1):230. https://doi.org/10.1186/s12951-024-02498-1
7. Wculek SK, Cueto FJ, Mujal AM, Melero I, Krummel MF, Sancho D. Dendritic cells in cancer immunology and immunotherapy. Nat Rev Immunol. 2020 Jan;20(1):7–24. https://doi.org/10.1038/s41577-019-0210-z
8. Jia X, Chen H, Wu M, Wang L, Li T, Ma J, et al. A biodegradable Antigen Nanocapsule promotes Anti-tumor Immunity via the cGAS-STING pathway. Adv Funct Mater. 2023 Jan12;33(10):2212085. https://doi.org/10.1002/adfm.202212085
9. Chu Y, Qian L, Ke Y, Feng X, Chen X, Liu F, et al. Lymph node-targeted neoantigen nanovaccines potentiate anti-tumor immune responses of post-surgical melanoma. J Nanobiotechnology. 2022 Apr 13;20(1):190. https://doi.org/10.1186/s12951-022-01397-7
10. Jin L, Yang D, Song Y, Li D, Xu W, Zhu Y, et al. In Situ Programming of Nanovaccines for Lymph Node-Targeted Delivery and Cancer Immunotherapy. ACS Nano. 2022 Sep 27;16(9):15226–15236. https://doi.org/10.1021/acsnano.2c06560
11. Wang Y, Zhao Q, Zhao B, Zheng Y, Zhuang Q, Liao N, et al. Remodeling Tumor-Associated Neutrophils to Enhance Dendritic Cell-Based HCC Neoantigen Nano-Vaccine Efficiency. Adv Sci (Weinh). 2022 Apr;9(11):e2105631. https://doi.org/10.1002/advs.202105631
12. Zhang H, Zhang Y, Hu H, Yang W, Xia X, Lei L, et al. In Situ Tumor Vaccine for Lymph Nodes Delivery and Cancer Therapy Based on Small Size Nanoadjuvant. Small. 2023 Aug;19(33):e2301041. https://doi.org/10.1002/smll.202301041
13. Du Bois H, Heim TA, Lund AW. Tumor-draining lymph nodes: At the crossroads of metastasis and immunity. Sci Immunol. 2021 Sep 10;6(63):eabg3551. https://doi.org/10.1126/sciimmunol.abg3551
14. Prokhnevska N, Cardenas MA, Valanparambil RM, Sobierajska E, Barwick BG, Jansen C, et al. CD8+ T cell activation in cancer comprises an initial activation phase in lymph nodes followed by effector differentiation within the tumor. Immunity. 2023 Jan 10;56(1):107–124.e5. https://doi.org/10.1016/j.immuni.2022.12.002
15. Barber A. Costimulation of Effector CD8+ T Cells: Which Receptor is Optimal for Immunotherapy? MOJ Immunol 2014;1(2):42–44. https://doi.org/10.15406/moji.2014.01.00011
16. Kamphorst AO, Pillai RN, Yang S, Nasti TH, Akondy RS, Wieland A, et al. Proliferation of PD-1+ CD8 T cells in peripheral blood after PD-1-targeted therapy in lung cancer patients. Proc Natl Acad Sci USA. 2017 May 9;114(19):4993–4998. https://doi.org/10.1073/pnas.1705327114
17. Sade-Feldman M, Yizhak K, Bjorgaard SL, Ray JP, de Boer CG, Jenkins RW, et al. Defining T Cell States Associated with Response to Checkpoint Immunotherapy in Melanoma. Cell. 2018 Nov 1;175(4):998–1013.e20. https://doi.org/10.1016/j.cell.2018.10.038
18. Miller BC, Sen DR, Al Abosy R, Bi K, Virkud YV, LaFleur MW, et al. Subsets of exhausted CD8+ T cells differentially mediate tumor control and respond to checkpoint blockade. Nat Immunol. 2019 Mar;20(3):326–336. https://doi.org/10.1038/s41590-019-0312-6
19. Jansen CS, Prokhnevska N, Master VA, Sanda MG, Carlisle JW, Bilen MA, et al. An intra-tumoral niche maintains and differentiates stem-like CD8 T cells. Nature. 2019 Dec;576(7787):465–470. https://doi.org/10.1038/s41586-019-1836-5
20. Blessin NC, Spriestersbach P, Li W, Mandelkow T, Dum D, Simon R, et al. Prevalence of CD8+ cytotoxic lymphocytes in human neoplasms. Cell Oncol (Dordr). 2020 Jun;43(3):421–430. https://doi.org/10.1007/s13402-020-00496-7
21. Dammeijer F, van Gulijk M, Mulder EE, Lukkes M, Klaase L, van den Bosch T, et al. The PD-1/PD-L1-Checkpoint Restrains T cell Immunity in Tumor-Draining Lymph Nodes. Cancer Cell. 2020 Nov 9;38(5):685–700.e688. https://doi.org/10.1016/j.ccell.2020.09.001
22. Connolly KA, Kuchroo M, Venkat A, Khatun A, Wang J, William I, et al. A reservoir of stem-like CD8+ T cells in the tumor-draining lymph node preserves the ongoing antitumor immune response. Sci Immunol. 2021 Oct;6(64):eabg7836. https://doi.org/10.1126/sciimmunol.abg7836

23. Jin M, Frankel WL. Lymph Node Metastasis in Colorectal Cancer. Surg Oncol Clin N Am. 2018 Apr;27(2):401–412. https://doi.org/10.1016/j.soc.2017.11.011
24. Inamori K, Togashi Y, Fukuoka S, Akagi K, Ogasawara K, Irie T, et al. Importance of lymph node immune responses in MSI-H/dMMR colorectal cancer. JCI Insight. 2021 May 10;6(9):e137365. https://doi.org/10.1172/jci.insight.137365
25. Koukourakis MI, Giatromanolaki A. Tumor draining lymph nodes, immune response, and radiotherapy: Towards a revisal of therapeutic principles. Biochim Biophys Acta Rev Cancer. 2022 May;1877(3):188704. https://doi.org/10.1016/j.bbcan.2022.188704
26. Okamura K, Nagayama S, Tate T, Chan HT, Kiyotani K, Nakamura Y. Lymphocytes in tumor-draining lymph nodes co-cultured with autologous tumor cells for adoptive cell therapy. J Transl Med. 2022 May 23;20(1):241. https://doi.org/10.1186/s12967-022-03444-1
27. Li Q, Zeng H, Liu T, Wang P, Zhang R, Zhao B, et al. A dendritic cell vaccine for both vaccination and neoantigen-reactive T cell preparation for cancer immunotherapy in mice. Nat Commun. 2024 Nov 29;15(1):10419. https://doi.org/10.1038/s41467-024-54650-y
28. Du Y, Song T, Wu J, Gao XD, Ma G, Liu Y, et al. Engineering mannosylated pickering emulsions for the targeted delivery of multicomponent vaccines. Biomaterials. 2022 Jan;280:121313. https://doi.org/10.1016/j.biomaterials.2021.121313
29. Wang J, Wang Y, Qiao S, Mamuti M, An H, Wang H. In situ phase transitional polymeric vaccines for improved immunotherapy. Natl Sci Rev. 2022 Feb;9(2):nwab159. https://doi.org/10.1093/nsr/nwab159
30. Scheetz L, Park KS, Li Q, Lowenstein PR, Castro MG, Schwendeman A, et al. Engineering patient-specific cancer immunotherapies. Nat Biomed Eng. 2019 Oct;3(10):768–782. https://doi.org/10.1038/s41551-019-0436-x
31. Qin H, Zhao R, Qin Y, Zhu J, Chen L, Di C, et al. Development of a Cancer Vaccine Using In Vivo Click-Chemistry-Mediated Active Lymph Node Accumulation for Improved Immunotherapy. Adv Mater. 2021 May;33(20):e2006007. https://doi.org/10.1002/adma.202006007
32. Kuai R, Ochyl LJ, Bahjat KS, Schwendeman A, Moon JJ. Designer vaccine nanodiscs for personalized cancer immunotherapy. Nat Mater. 2017 Apr;16(4):489–496. https://doi.org/10.1038/nmat4822
33. Sahin U, Türeci Ö. Personalized vaccines for cancer immunotherapy. Science. 2018 Mar 23;359(6382):1355–1360. https://doi.org/10.1126/science.aar7112
34. Keskin DB, Anandappa AJ, Sun J, Tirosh I, Mathewson ND, Li S, et al. Neoantigen vaccine generates intratumoral T cell responses in phase Ib glioblastoma trial. Nature. 2019 Jan;565(7738):234–239. https://doi.org/10.1038/s41586-018-0792-9
35. Wang H, Mooney DJ. Biomaterial-assisted targeted modulation of immune cells in cancer treatment. Nat Mater. 2018 Sep;17(9):761–772. https://doi.org/10.1038/s41563-018-0147-9
36. Yu X, Dai Y, Zhao Y, Qi S, Liu L, Lu L, et al. Melittin-lipid nanoparticles target to lymph nodes and elicit a systemic anti-tumor immune response. Nat Commun. 2020 Feb 28;11(1):1110. https://doi.org/10.1038/s41467-020-14906-9
37. Zhou L, Zhao L, Wang M, Qi X, Zhang X, Song Q, et al. Dendritic Cell-Hitchhiking In Vivo for Vaccine Delivery to Lymph Nodes. Adv Sci (Weinh). 2024 Sep;11(33):e2402199. https://doi.org/10.1002/advs.202402199
38. Liu M, Feng Y, Lu Y, Huang R, Zhang Y, Zhao Y, et al. Lymph-targeted high-density lipoprotein-mimetic nanovaccine for multi-antigenic personalized cancer immunotherapy. Sci Adv. 2024 Mar 15;10(11):eadk2444. https://doi.org/10.1126/sciadv.adk2444
39. Dong H, Su H, Chen L, Liu K, Hu HM, Yang W, et al. Immunocompetence and mechanism of the DRibble-DCs vaccine for oral squamous cell carcinoma. Cancer Manag Res. 2018;10:493–501. https://doi.org/10.2147/CMAR.S155914
40. Zhang M, Hong JA, Kunst TF, Bond CD, Kenney CM, Warga CL, et al. Randomized phase II trial of a first-in-human cancer cell lysate vaccine in patients with thoracic malignancies. Transl Lung Cancer Res. 2021 Jul;10(7):3079–3092. https://doi.org/10.21037/tlcr-21-1
41. Tanyi JL, Bobisse S, Ophir E, Tuyaerts S, Roberti A, Genolet R, et al. Personalized cancer vaccine effectively mobilizes antitumor T cell immunity in ovarian cancer. Sci Transl Med. 2018 Apr 11;10(436):eaao5931. https://doi.org/10.1126/scitranslmed.aao5931
42. Hosseini R, Sarvnaz H, Arabpour M, Ramshe SM, Asef-Kabiri L, Yousefi H, et al. Cancer exosomes and natural killer cells dysfunction: biological roles, clinical significance and implications for immunotherapy. Mol Cancer. 2022 Jan 14;21(1):15. https://doi.org/10.1186/s12943-021-01492-7

43. Rao Q, Zuo B, Lu Z, Gao X, You A, Wu C, et al. Tumor-derived exosomes elicit tumor suppression in murine hepatocellular carcinoma models and humans in vitro. Hepatology. 2016 Aug;64(2):456–472. https://doi.org/10.1002/hep.28549
44. Xu J, Liu H, Wang T, Wen Z, Chen H, Yang Z, et al. CCR7 Mediated Mimetic Dendritic Cell Vaccine Homing in Lymph Node for Head and Neck Squamous Cell Carcinoma Therapy. Adv Sci (Weinh). 2023 Jun;10(17):e2207017. https://doi.org/10.1002/advs.202207017
45. Goswami S, Anandhan S, Raychaudhuri D, Sharma P. Myeloid cell-targeted therapies for solid tumours. Nat Rev Immunol. 2023 Feb;23(2):106–120. https://doi.org/10.1038/s41577-022-00737-w
46. Perez CR, De Palma M. Engineering dendritic cell vaccines to improve cancer immunotherapy. Nat Commun. 2019 Nov 27;10(1):5408. https://doi.org/10.1038/s41467-019-13368-y
47. Kvedaraite E, Ginhoux F. Human dendritic cells in cancer. Sci Immunol. 2022 Apr;7(70):eabm9409. https://doi.org/10.1126/sciimmunol.abm9409
48. Sprooten J, Vanmeerbeek I, Datsi A, Govaerts J, Naulaerts S, Laureano RS, et al. Lymph node and tumor-associated PD-L1+ macrophages antagonize dendritic cell vaccines by suppressing CD8+ T cells. Cell Rep Med. 2024 Jan 16;5(1):101377. https://doi.org/10.1016/j.xcrm.2023.101377
49. Wang R, Zhu T, Hou B, Huang X. An iPSC-derived exosome-pulsed dendritic cell vaccine boosts antitumor immunity in melanoma. Mol Ther. 2023 Aug 2;31(8):2376–2390. https://doi.org/10.1016/j.ymthe.2023.06.005
50. Ghasemi A, Martinez-Usatorre A, Li L, Hicham M, Guichard A, Marcone R, et al. Cytokine-armed dendritic cell progenitors for antigen-agnostic cancer immunotherapy. Nat Cancer. 2024 Feb;5(2):240–261. https://doi.org/10.1038/s43018-023-00668-y

Information about authors:

Elena M. Frantsiyants – Dr. Sci. (Biol.), Professor, Deputy Director General for Scientific Work, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation
ORCID: https://orcid.org/0000-0003-3618-6890, SPIN: 9427-9928, AuthorID: 462868, ResearcherID: Y-1491-2018, Scopus Author ID: 55890047700

Valeriya A. Bandovkina ✉ – Dr. Sci. (Biol.), senior researcher at the Laboratory for the Study of Pathogenesis of Malignant Tumors, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation
ORCID: https://orcid.org/0000-0002-2302-8271, SPIN: 8806-2641, AuthorID: 696989, ResearcherID: AAG-8708-2019, Scopus Author ID: 57194276288

Tatiana I. Moiseenko – Dr. Sci. (Med.), Professor, chief researcher, Section of Reproductive Tumors, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation
ORCID: https://orcid.org/0000-0003-4037-7649, SPIN: 6341-0549, AuthorID: 705829

Yuliya A. Petrova – Cand. Sci. (Biol.), senior researcher, Laboratory of Study of Malignant Tumor Pathogenesis, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation
ORCID: https://orcid.org/0000-0002-2674-9832, SPIN: 2168-8737, AuthorID: 558241, ResearcherID: AAE-4168-2022, Scopus Author ID: 37026863400

Irina A. Goroshinskaya – Dr. Sci. (Biol.), Professor, senior researcher at Laboratory of Malignant Tumor Pathogenesis Study, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation
ORCID: https://orcid.org/0000-0001-6265-8500, SPIN: 9070-4855, Author ID: 79968, ResearcherID: Y-2277-2018, Scopus Author ID: 6602191458

Galina V. Zhukova – Dr. Sci. (Biol.), senior researcher at Laboratory of Malignant Tumor Pathogenesis Study, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation
ORCID: https://orcid.org/0000-0001-8832-8219, SPIN: 1887-7415, Author ID: 564827, ResearchID: Y-4243-2016, Scopus Author ID: 7005456284

Lidiya K. Trepitaki – Cand. Sci. (Biol.), researcher at the Laboratory for the Study of Pathogenesis of Malignant Tumors, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation
ORCID: https://orcid.org/0000-0002-9749-2747, SPIN: 2052-1248, AuthorID: 734359, ResearcherID: AAG-9218-2019, Scopus Author ID: 55357624700

Ekaterina I. Surikova – Cand. Sci. (Biol.), senior researcher at the Laboratory for the Study of Pathogenesis of Malignant Tumors, National Medical Research Centre for Oncology, Rostov-on-Don, Russian Federation
ORCID: https://orcid.org/0000-0002-4318-7587, SPIN: 2401-4115, AuthorID: 301537, ResearcherID: AAG-8748-2019, Scopus Author ID: 6507092816

Contribution of the authors:

Frantsiyants E. M. – scientific management, writing the draft;
Bandovkina V. A. – follow on revision of the text, final conclusion;
Moiseenko T. I. – research concept, follow on revision of the text;
Petrova Yu. A. – research concept, follow on revision of the text;
Goroshinskaya I. A. – research concept, follow on revision of the text;
Zhukova G. V. – research concept, follow on revision of the text;
Trepitaki L. K. – research concept, follow on revision of the text;
Surikova E. I. – follow on revision of the text, final conclusion.