Journal of Organic and Pharmaceutical Chemistry

MiniReview

OPEN ACCESS
Freely available online on
http://ophcj.nuph.edu.ua

UDC 615.032:616-00.03.06.08

O. F. Piminov, R. V. Sahaidak-Nikitiuk, A. I. Kvitchata, S. M. Rolik-Attia
Institute for Advanced Training of Pharmacy Specialists of the National University of Pharmacy of the Ministry of Health of Ukraine, 17 Zakhysnykiv Ukrainy sq., 61001 Kharkiv, Ukraine

Immunotherapy of Diseases and Nanotechnology: Current State and Prospects

Abstract
Nanotechnology can be used to treat a number of diseases, which are currently the main cause of death in the world, and allow to achieve the desired therapeutic effect for the patient. This mini-review focuses on the analysis of scientific literary sources dealing with the application of nanotechnology in the immunotherapy of diseases and covers the period from 2016 to 2022. In particular, it provides an overview of recently discovered nanotechnologies (including immunomodulatory nanosystems) used for the prevention and treatment of various diseases, including cancer, infectious, inflammatory, and autoimmune diseases. The review also discusses the role of nanosystems in cancer immunotherapy. Additional attention is paid to nanomaterials with new structures, properties, and functions, which are used in the modern practice of treating viral and bacterial infections. A part of the paper is devoted to nanoparticles that enhance the effect of immunosuppressive cells in the treatment of inflammatory and autoimmune diseases. The analysis performed clearly demonstrates the relevance of nanotechnologies for the use in the immunotherapy of diseases. We hope it will allow researchers to identify new areas for using nanoparticles in the treatment of diseases of various etiologies.
Keywords: nanosystem; nanotechnology; nanoparticle; nanomaterials; autoimmune disease; disease treatment

О. Ф. Пімінов, Р. В. Сагайдак-Нікітюк, А. І. Квітчата, С. М. Ролік-Аттіа
Інститут підвищення кваліфікації спеціалістів фармації Національного фармацевтичного університету Міністерства охорони здоров'я України,
майдан Захисників України, 17, Харків, 61001, Україна

Імунотерапія захворювань та нанотехнології: сучасний стан та перспективи

Анотація
Нанотехнології можна використовувати для лікування певних захворювань, що сьогодні є основною причиною смертності у світі, бо це дозволяє досягти необхідного терапевтичного ефекту для пацієнта. Цей міні-огляд, що охоплює період з 2016 до 2022 рр., зосереджено на аналізі наукових літературних джерел, у яких висвітлено застосування нанотехнологій в імунотерапії захворювань. Йдеться, зокрема, про нещодавно відкриті нанотехнології (разом з імуномодулювальними наносистемами), що їх застосовують для профілактики і лікування раку, інфекційних, запальних та аутоімунних захворювань. Розглянуто особливості використання в сучасній практиці лікування вірусних і бактеріальних інфекцій наноматеріалів з новими структурами, властивостями та функціями. Схарактеризовано наночастинки, які посилюють дію імуносупресивних клітин у лікуванні запальних та аутоімунних захворювань. Проведений аналіз наочно демонструє актуальність нанотехнологій для імунотерапії захворювань і, сподіваємось, дозволить дослідникам визначити нові напрями використання наночастинок у лікуванні захворювань різної етіології.
Ключові слова: наносистема; нанотехнологія; наночастинка; наноматеріали; аутоімунні захворювання; лікування захворювань

Citation: Piminov, O. F.; Sahaidak-Nikitiuk, R. V.; Kvitchata, A. I.; Rolik-Attia, S. M. Immunotherapy of Diseases and Nanotechnology: Current State and Prospects. *Journal of Organic and Pharmaceutical Chemistry* **2024**, *22* (1), 13–21.
https://doi.org/10.24959/ophcj.24.304776
Received: *27 March 2024*; **Revised:** *13 April 2024*; **Accepted:** *17 April 2024*

Funding: The authors received no specific funding for this work.
Conflict of interests: The authors have no conflict of interests to declare.

Introduction

Today, immunotherapy has evolved into an effective strategy for the prevention and treatment of various diseases, including cancer, infectious, inflammatory, and autoimmune diseases. Immunomodulatory nanosystems can easily improve therapeutic effects while simultaneously overcoming many barriers to treatment, such as inadequate immune stimulation, side effects, and the loss of bioactivity of immune agents during circulation. In recent years, researchers have been constantly developing nanomaterials with new structures, properties and functions.

In cancer immunotherapy, nanosystems play an important role in activating immune cells and modulating the tumor microenvironment, as well as in combination with other antitumor approaches.

Regarding infectious diseases, there are many promising results of using vaccines made of nanomaterials against viral and bacterial infections. In addition, nanoparticles also enhance the effect of immunosuppressive immune cells in the treatment of inflammatory and autoimmune diseases.

A human immune system is able to protect them from many diseases based on a process called "immune surveillance". In theory, viruses, bacteria and cancer cells can be quickly identified as foreign antigens and eliminated by immune cells. However, pathogens have developed a number of effective mechanisms to evade immune clearance by inhibiting phagocytosis, blocking antigen presentation, or directly killing immune cells. Cancer cells can shift the tumor microenvironment (TME) into a highly immunosuppressive state by recruiting immunosuppressive immune cells and expressing a series of inhibitory cytokines, enzymes, and checkpoint molecules, thereby promoting tumor immune evasion. These barriers certainly reduce the efficiency and intensity of immune responses. Conversely, aberrant activation of immune cells can cause uncontrolled inflammatory, autoimmune or allergic diseases. Abnormal inflammation can also lead to the transplant rejection and hinder the regeneration of tissues and organs, so therapeutic interventions are necessary to maintain the homeostasis and function of the immune system [1].

Results and discussion

Nanotechnology can solve the existing problems and thus achieve the desired therapeutic effect. Studies have shown that nanoplatforms exhibit many useful properties, including co-delivery of antigens and adjuvants to the same antigen-presenting cells (APC) or intracellular compartments [2]; increased half-life of bioactive cargo molecules due to prevention of decomposition by enzymes during blood circulation; increased accumulation in tumor tissues due to the size-dependent effect of the enhanced permeability and retention (EPR) [3]; surface modification to certain target tissues or cells [4]; the stimulus-sensitive behavior for safe circulation and intelligent drug release [5, 6]; more tolerable doses due to less accumulation in non-target organs and tissues [7]; the surface binding of both antigens and costimulatory molecules to create of artificial APC (aAPC) for powerful T-cell activation [8]; various routes of drug delivery, such as intranasal administration or subcutaneous delivery using a patch with microneedles [2, 9]; internal immunomodulatory functions of created nanoparticles [10].

Researchers have synthesized nanoparticles with different structures and biological functions for drug delivery. Some of the most commonly used nanosystems are polymer nanoparticles [11, 12], liposomes [13, 14], micelles [15, 16], nanogels [4, 17, 18], gold nanoparticles [19, 20] and carbon nanomaterials [21]. These nanoplatforms have demonstrated phenomenal capabilities in facilitating the immunostimulatory or immunosuppressive regulation through targeted delivery and controlled release of antigens, adjuvants and immunoregulatory agents in response to a stimulus. One of the strategies to improve the localization of encapsulated cargoes in tissues or target cells is the chemical modification of nanoparticles with target fragments. For example, nanomaterials decorated with a DEC-205 antibody (Ab), CD40 Ab, CDllc Ab or mannose can be internalized predominantly by dendritic cells (DC) *via* the receptor-mediated endocytosis [22, 23]. Similarly, folic acid, lectins, and CD44 are used to recognition by the corresponding receptors overexpressed on macrophages [24]. The surface binding of CD3 Ab or tLypl peptide showed an increased uptake by T-cells and regulatory T-cells (Treg), respectively [25, 26]. In addition, nanoplatforms consisting of dextran or dextran sulfate have intrinsic properties of targeting macrophages [27].

Researchers have devoted considerable attention to the specific functionalization of nanoparticles in the treatment of a wide range of diseases where nanoparticles act as the main component rather than delivery vehicles. In particular, in

ISSN 2308-8303 (Print) / 2518-1548 (Online)

tumor immunotherapy, stimuli-sensitive nanomaterials are being developed to maintain the structural integrity in the serum and promote the release of a specific payload in TME [28, 29]. Internal and external stimulus – responsive strategies (pH [6, 30, 31], reduction [5, 32], enzymes [14, 33] light [34], heat and reactive oxygen species (ROS) [35]) are involved in creation of nanoparticles and achieved an improved antitumor effect. In addition, other antitumor molecules and agents can be added to these nanoplatforms for the synergistic combination therapy.

It should be noted that in the last few decades, immunotherapy has become a rapidly growing method of cancer treatment [36, 37]. Unlike chemotherapy, radiation therapy and surgery, it aims to activate immune cells to identify and destroy tumor cells. In this way, side effects on normal organs and tissues can be significantly reduced. Moreover, the immunotherapeutic strategy also provides long-term protection against tumor recurrence due to the induction of the immunological memory [38].

Recently, much attention has been paid to the immune checkpoint blockade therapy targeting cytotoxic T-lymphocyte antigen 4 (CTLA-4), programmed cell death 1 (PD-1) or ligand, cell death 1 (PD-L1), negative regulation of T-lymphocytes [39]. Adoptive cell transfer (ACT), especially chimeric antigen receptor (CAR)-T therapy using *ex vivo* expanded and genetically engineered T-cells for antigen-specific tumor therapy, has also recently been approved by the United States Food and Drug Administration (FDA) for B-cells and therapy of non-Hodgkin's lymphoma [40]. Based on the results obtained, the effectiveness of cancer immunotherapy can be further improved with the help of nanotechnology. However, immunotherapeutic treatments for solid tumors are limited due to the strong immunosuppressive TME, as well as the abnormal extracellular matrix. More seriously, the "off-target" effects of immunomodulatory agents can cause damage to normal tissues and cells.

Today, nanotechnology has been proven to improve the therapeutic efficacy of cancer immunotherapy mainly due to three aspects:

- protection of antigens and adjuvants, especially in the case of nucleic acid;
- effective delivery to APC and initiation of a powerful tumor antigen-specific immune response;
- reprogramming of the TME to restore immune surveillance.

Recently, a large number of nanoparticle-based delivery systems aimed at modulating immune cells have been developed for cancer treatment [41, 42] and some of them have undergone various stages of clinical trials [43], confirming their great therapeutic potential as anticancer agents. For example, during *Phase III* clinical trials, non-small cell lung cancer (NSCLC) patients vaccinated with tecemotide (L-BLP25) containing the immunoadjuvant monophosphoryl lipid A and synthetic mucin 1 lipopeptide (MUC1) showed an increased three-year survival rate of 49% compared to 27% of patients receiving only maintenance therapy. In addition, it should be noted that another 12 new liposomal drugs for the treatment of cancer patients developed by various manufacturers (Merck, Oncothyreon Canada Inc., Biontech RNA Pharmaceutical, GlaxoSmithKline, Lipotec Pty Ltd.) are completing clinical trials. GlaxoSmithKline also developed a liposomal drug for the treatment of malaria; Crucell Berna Biotech LTD – liposomes for the treatment of hepatitis A; Statens Serum Inst. – a liposomal drug for the treatment of tuberculosis; Biotherapeutics Inc., Crucell Bema Biotech Ltd., CSL Biotherapies are studying virosomal drugs against influenza. To achieve accurate and controlled drug delivery, smart nanoparticles with more complex structure and special drug release properties are also produced according to the distinctive features of TME, such as slightly acidic pH (6.5–6.8), high levels of glutathione and hydrogen peroxide (H_2O_2), disruption of the production of proteinases, such as matrix metalloproteinase-2 (MMP-2) [33, 44].

Recently, advances in the field of nanotechnology have stimulated the study of a large number of nanomaterials for the activation and maturation of APC. Liposomes are the most favorable material of immunotherapeutic nanosystems for clinical use due to the lack of toxicity and immunogenicity, Lipo-MERIT, iscomatrix, Lipovaxin MM, etc. It has been proven that, in addition to liposomes, some other nanomaterials are safe for the human. For example, Oncoquest-L, an anti-cancer vaccine undergoing phase I clinical trials, is made from an extract of the patient's own cancer cells, and IL-2 is delivered by proteoliposomes. Two cholesteryl pullulan-based cancer vaccines, CHP-NY-ESO-1 and CHP-HER2, elicited antigen-specific immune responses against NY-ESO-1 and HER2 in the presence of adjuvant OK-432 in esophageal cancer patients [45].

Nanomaterials, such as PLGA, iron oxide nanoparticles, virus-like particles (VLP) and conjugated polymers, can enhance the uptake of APC cells and stimulate the immune response [46]. Meian-A VLP used for the treatment of stage III-IV malignant melanoma is in phase III clinical trials [47]. The VLP Melan-A vaccine composed of a protein coat derived from bacteriophage Qbeta, CpG, and a peptide antigen from melanoma cells elicited greater than twofold increase in antigen-specific T-cell responses in 76% of patients. In some other cases, nanoparticles are also designed as an important component of the final product in order to facilitate the effect of tumor antigens on the host immune system.

Another strategy avoids the need to escape from endosomes and provides efficient T-cell activation and tumor eradication by designing aAPC based on the modification of nanosized particles, including magnetic beads, liposomes, polymeric and paramagnetic nanoparticles [48, 49]. aAPC mainly contain two signals for the T-cell activation, that is, the MHCI-antigen complex and a costimulatory signal, such as anti-CD28 and anti-CD3 Abs [50]. They can be administered intravenously *in vivo* or used in ACT *ex vivo*.

Many studies conducted in recent years have shown that combining immunotherapy with other anticancer approaches, such as chemotherapy, phototherapy, and radiation therapy, has a synergistic effect and significantly improves therapeutic efficacy against a wide range of malignancies [51, 52]. Chemotherapeutic agents or external influences (light and radiation) not only directly destroy tumors, but participate in the immune process, causing the death of immunogenic (ICD) tumor cells.

The concept of ICD proposed in recent years demonstrates that dying tumor cells (DTCs) can generate a mass of antigens and increase the formation of damage-associated molecular patterns (DAMP), such as adenosine triphosphate, CRT, heat shock proteins and high mobility groups. DAMP provide the "*eat me*" signals for antigen recognition and phagocytosis by DC and trigger the activation of the adaptive immune response [53]. More importantly, ICD-derived tumor antigens can be controlled by the immune system and pose threat to abscopal and metastatic tumors, which is called the "abscopal effect" [51, 54].

Chemotherapy is the preferred therapeutic regimen in the clinic, but its application is seriously hampered by its notorious side effects and tumor recurrence. Chemotherapy in combination with immunotherapy can reduce toxicity and improve the therapeutic effect. In chemoimmunotherapy, low-dose chemotherapy is able to induce ICD of tumor cells and lead to the release of tumor antigen, thus preventing serious side effects. At the same time, immunoregulatory agents provide a favorable environment for highly efficient antigen presentation and activation of APC and cytotoxic T-cells. Many studies, in which chemo/immunotherapeutic agents are encapsulated in nanoscale drug delivery systems, have been successful [13, 39, 55].

For example, the FEN group [13] loaded the TLR9 agonist CpG into a nanodepot platform (NDP) consisting of cationic liposomes and thiolated hyaluronic acid. CpG-NDP was then conjugated to the surface of immunogenic DTC induced by mitoxantrone, an anthracenedione antitumor agent. The experiment showed that DTC-CpG-NDP vaccination significantly stimulated the generation of tumor antigen-specific CD8+T cells and strongly protected against melanoma infection.

It should be noted that some of the traditional chemotherapeutic agents unexpectedly exert an immunoregulatory effect on immune cells. For example, the chemotherapeutic drug paclitaxel (PTX) has a modulating effect on the polarization of macrophages according to the ML-based phenotype at low concentrations [56]. Unlike free PTX, NP-PTX can be efficiently endocytosed by macrophages and stimulate the macrophage polarization in a dose-dependent manner without causing obvious toxicity to immune cells. Although the mechanism underlying this phenomenon is not fully understood, it represents an unconventional strategy for investigating the immunomodulatory function of chemotherapeutic agents.

Many attractive characteristics of nanoparticles in cancer immunotherapy are also applicable to prevent or counteract bacterial and viral infections, such as human immunodeficiency virus (HIV), influenza, encephalitis, hepatitis, Ebola, pneumonia, etc. [7, 57]. For the prevention of these diseases, anti-infective vaccines used certain antigenic components instead of whole microbes to increase the immune efficiency. However, these antigens are more easily broken down by enzymes and removed from the bloodstream. Moreover, they usually require the help of adjuvants to effectively activate the immune system. In addition, DNA vaccines have also shown a great potential in recent years, but their use in clinical practice is limited due to their low

ISSN 2308-8303 (Print) / 2518-1548 (Online)

safety and efficacy. Nanotechnology opens up the possibilities of a new generation of anti-infective vaccines. Currently, nanovaccines based on virosomes and liposomes against infectious diseases have shown good effectiveness. Two nanoparticle-based vaccines, Inflexal V and Epaxal, are FDA approved for the prevention of malaria, influenza and hepatitis A. Nanoparticles of appropriate size can deliver antigens and adjuvants to immune cells by encapsulation or surface conjugation. Nanoparticles are also designed as a reservoir for the slow release of antigens to increase the exposure of APC. For DNA vaccines, nanoparticles provide a non-viral delivery strategy that transports genetic material in a site-specific manner. Ample evidence has supported the promising effects of nanotechnology-based vaccines against infectious diseases, which benefit from the improved delivery efficiency, convenient nanoparticle engineering and the intrinsic adjuvant function. Immunomodulatory systems using nanoparticles for the prevention and treatment of infectious diseases include a vaccine with nanoparticles against HIV, influenza, bacterial infection and other infectious diseases.

Nanoparticles, including inorganic and polymeric nanoparticles, as effective delivery vehicles have shown effective immunization to protect against bacteria and infections. Thus, gold nanoparticles are better for preparing a nanovaccine due to good biocompatibility, a simple synthesis process and, most importantly, the adjuvant activity. For example, gold nanoparticles conjugated to *Pseudomonas aeruginosa* flagellin showed antibody titer against flagellin compared to flagellin formulated in Freund's adjuvant [58]. In another study, *Vetro et al.* [59] developed a glycoconjugate nanoparticle vaccine that modified gold nanoparticles with pneumococcal capsular polysaccharide antigens, which were an important component of the current commercial vaccine and also required for pneumococcal infection. A glucose derivative was added as an internal component of the gold nanoparticles to increase water solubility, and the T-helper peptide OVA was also loaded on to the gold nanoparticles. This glycoconjugate vaccine induced a potent and specific IgG-Ab-dependent immune response against *Streptococcus pneumoniae* in mice. Many other studies have highlighted the improved outcome of fighting infections due to the use of nanotechnology for the delivery of antigen and/or adjuvants [60, 61]. Next, it is interesting to focus on the design and application of biomimetic nanoparticles with a modified surface as a vaccine against bacterial infection. Nanoparticle platforms, designed with their inherent ability to neutralize toxins and enhance immunity, have superior properties over traditional methods due to the increased safety and more efficient removal of toxins or antigens.

The next area of improving medicine is the development of DNA vaccination. However, despite the low cost and rapid production of DNA vaccines, their low stability and insufficient immunogenicity limit their use in the prevention and treatment of various infectious diseases. Nanotechnology provides a new opportunity in the development of nanoparticle platforms containing DNA vaccines for controlled and targeted delivery to specific cells. *Draz et al.* [57] reported DNA vaccination against a model hepatitis C virus using plasma gold nanoparticles that could be activated by specific electrical pulses to facilitate pore formation in the adjacent cell membrane and increase membrane permeability for DNA transfection. In this case, the absorption of the DNA vaccine by myocytes significantly increases after the joint administration of the free DNA plasmid and gold nanoparticles to the animals, which allowed more efficient expression of the encoded genes. Moreover, due to the low electric field required for this process, cell destruction or lysis can be avoided.

In addition to the ability to enhance the pro-inflammatory immune response, nanoparticle platforms have also been used to induce immune tolerance against chronic or acute inflammation, autoimmune diseases, transplant rejection and allergy. Unlike cancer and infections, which enter the human body through an insufficient immune response, these diseases arise as a result of an improper overreaction of the immune system to autoantigens, allogeneic antigens during transplantation, or environmental factors. Considering the fact that nanotechnological immunostimulation has attracted much attention, monitoring the immunosuppressive properties of nanomaterials is equally important to alleviate the immune-mediated burden. Immunosuppressants, mostly with small molecules, have shown improved therapeutic efficacy in recent years. However, long-term treatment can lead to severe systemic toxicity or immunodeficiency [62]. Many immunosuppressants, such as methotrexate, rapamycin and dexamethasone, are hydrophobic drugs and have a limited biological activity. These agents are randomly and widely

distributed in the body after introduction, leading to serious side effects in non-target tissues and causing damage of the liver, muscles and the gastrointestinal tract.

Anti-inflammatory cytokines, such as IL-4, have been widely studied in the treatment of various autoimmune diseases. However, their short half-life determines the introduction of high doses and inevitable systemic toxicity. The therapeutic delivery of microRNAs (miRNAs) for symptom control can also be challenging due to limited efficacy, low stability, and the lack of targeting. Nanotechnology overcomes the existing shortcomings of immunosuppressants through multiple aspects, such as providing protection against degradation, prolonging blood circulation and facilitating the immune cell-targeted delivery [63]. The nanoparticle itself can also be converted into an immunomodulatory component, and nanoparticles delivering the antigen-MHC complex can expand antigen-specific Treg to control inflammatory disorders.

■ Conclusions

Nanotechnology opens up great opportunities for the prevention and treatment of infectious diseases since the coded delivery of antigens and adjuvants significantly increases the immunogenicity of microbial components and demonstrates higher efficacy than conventional vaccines using whole microbes.

Thus, nanomaterial-based immunotherapy is rapidly developing and will show significant potential over the past few decades. Thanks to constantly improved production methods and design strategies, nanotechnology is successfully used to control and prevent many diseases through immune regulation. As discussed above, the data presented highlight excellent tumor treatment outcomes due to the activation of APC and T-cells, regulation of Treg, TAM and MDSC in immunosuppressive TME and the synergism with chemotherapy, phototherapy and radiotherapy. In the prevention and eradication of infectious viruses and bacteria, the nanoparticle-based vaccine provides higher absorption of APC and induces improved T and B cell responses. In addition, the coded delivery of tumor antigens and adjuvants in nanosized carriers increases the effectiveness of anticancer vaccines. A new trend in cancer immunotherapy involves the recognition of tumor neoantigens, which originate from patient-specific cancer mutations and can be identified as "foreign" by the immune system. Although a tumor neoantigen may be an ideal candidate for personalized cancer immunotherapy, it is rare in some cancers with low mutations, and therefore, a combination with radiation therapy or chemotherapy is preferable to increase the burden of mutations, as well as tumor neoantigens. In addition, the process of identification and synthesis of neoantigen peptides is time-consuming, and new techniques and methods are urgently needed to reduce this time period [64].

Then nanomaterials have emerged as a new antibacterial weapon in addition to antibiotics in protecting against various microbial infections, including resistant bacteria. It is known that nanomaterials cause lethality in two ways, namely, the destruction of cell membranes and the production of ROS. However, it has been found that nanomaterials have the increased antimicrobial activity with lower toxicity and do not cause drug resistance compared to antibiotics.

■ References

1. Pearson, R. M.; Casey, L. M.; Hughes, K. R.; Miller, S. D.; Shea, L. D. *In vivo* reprogramming of immune cells: Technologies for induction of antigen-specific tolerance. *Adv. Drug Deliv. Rev.* **2017**, *114*, 240–255. https://doi.org/10.1016/j.addr.2017.04.005.
2. Tazaki, T.; Tabata, K.; Ainai, A.; Ohara, Y.; Kobayashi, S.; Ninomiya, T.; Orba, Y.; Mitomo, H.; Nakano, T.; Hasegawa, H.; Ijiro, K.; Sawa, H.; Suzuki, T.; Niikura, K. Shape-dependent adjuvanticity of nanoparticle-conjugated RNA adjuvants for intranasal inactivated influenza vaccines. *RSC Adv.* **2018,** *8* (30), 16527–16536. https://doi.org/10.1039/C8RA01690A.
3. Kim, H.; Niu L.; Larson, P.; Kucaba, T. A.; Murphy, K. A.; James, B. R.; Ferguson, D. M.; Griffith, T. S.; Panyam, J. Polymeric nanoparticles encapsulating novel TLR7/8 agonists as immunostimulatory adjuvants for enhanced cancer immunotherapy. *Biomaterials* **2018**, *164*, 38–53. https://doi.org/10.1016/j.biomaterials.2018.02.034.
4. Chen, J.; Ding, J.; Xu, W.; Sun, T.; Xiao, H.; Zhuang, X.; Chen, X. Receptor and Microenvironment Dual-Recognizable Nanogel for Targeted Chemotherapy of Highly Metastatic Malignancy. *Nano Lett*. **2017**, *17* (7), 4526–4533. https://doi.org/10.1021/acs.nanolett.7b02129.
5. Xu, W.; Ding, J.; Chen, X. Reduction-Responsive Polypeptide Micelles for Intracellular Delivery of Antineoplastic Agent. *Biomacromolecules* **2017**, *18* (10), 3291–3301. https://doi.org/10.1021/acs.biomac.7b00950.
6. Zhang, Y.; Cai, L.; Li, D.; Lao, Y.-H.; Liu, D.; Li, M.; Ding, J.; Chen, X. Tumor microenvironment-responsive hyaluronate-calcium carbonate hybrid nanoparticle enables effective chemotherapy for primary and advanced osteosarcomas. *Nano Res.* **2018,** *11* (9), 4806–4822. https://doi.org/10.1007/s12274-018-2066-0.
7. Gao, S.; Tang, G.; Hua, D.; Xiong, R.; Han, J.; Jiang, S.; Zhang, Q.; Huang, C. Stimuli-responsive bio-based polymeric systems and their applications. *J. Mater. Chem. B* **2019**, *7* (5), 709–729. https://doi.org/10.1039/c8tb02491j.

ISSN 2308-8303 (Print) / 2518-1548 (Online)

8. Musetti, S.; Huang, L. Nanoparticle-Mediated Remodeling of the Tumor Microenvironment to Enhance Immunotherapy. *ACS Nano* **2018**, *12* (12), 11740–11755. https://doi.org/10.1021/acsnano.8b05893.
9. Yang, H.-W.; Ye, L.; Guo, X. D.; Yang, C.; Compans, R. W.; Prausnitz, M. R. Ebola Vaccination Using a DNA Vaccine Coated on PLGA-PLL/γPGA Nanoparticles Administered Using a Microneedle Patch. *Adv. Healthcare Mater.* **2017,** *6* (1), 1600750. https://doi.org/10.1002/adhm.201600750.
10. Li, S.; Feng, X.; Wang, J.; He, L.; Wang, C.; Ding, J.; Chen, X. Polymer nanoparticles as adjuvants in cancer immunotherapy. *Nano Res.* **2018,** *11* (11), 5769–5786. https://doi.org/10.1007/s12274-018-2124-7.
11. Xiao, H.; Yan, Lesan; Dempsey, E. M.; Song, W.; Qi, R.; Li, W.; Huang, Y.; Jing, X.; Zhou, D.; Ding, J.; Chen, X. Recent progress in polymer-based platinum drug delivery systems. *Prog. Polym. Sci.* **2018**, *87*, 70–106. https://doi.org/10.1016/j.progpolymsci.2018.07.004.
12. Wang, Y.; Jiang, Z.; Xu, W.; Yang, Y.; Zhuang, X.; Ding, J.; Chen, X. Chiral Polypeptide Thermogels Induce Controlled Inflammatory Response as Potential Immunoadjuvants. *ACS Appl. Mater. Interfaces* **2019**, *11* (9), 8725–8730. https://doi.org/10.1021/acsami.9b01872.
13. Fan, Y.; Kuai, R.; Xu, Y.; Ochyl, L. J.; Irvine, D. J.; Moon, J. J. Immunogenic Cell Death Amplified by Co-localized Adjuvant Delivery for Cancer Immunotherapy. *Nano Lett.* **2017**, *17* (12), 7387–7393. https://doi.org/10.1021/acs.nanolett.7b03218.
14. Song X.; Xu J.; Liang C.; Chao Y.; Jin Q.; Wang C.; Chen M.; Liu Z. Self-Supplied Tumor Oxygenation through Separated Liposomal Delivery of H_2O_2 and Catalase for Enhanced Radio-Immunotherapy of Cancer. *Nano Lett*. **2018**, *18* (10), 6360–6368. https://doi.org/10.1021/acs.nanolett.8b02720.
15. He, L.; Xu, W.; Wang, X.; Wang, C.; Ding, J.; Chen, X. Polymer micro/nanocarrier-assisted synergistic chemohormonal therapy for prostate cancer. *Biomater. Sci.* **2018**, 6, 1433–1444. https://doi.org/10.1039/C8BM00190A.
16. Wang, J.; Xu, W.; Li, S.; Qiu, H.; Li, Z.; Wang, C.; Wang X., Ding, J. Polylactide-Cholesterol Stereocomplex Micelle Encapsulating Chemotherapeutic Agent for Improved Antitumor Efficacy and Safety. *J. Biomed. Nanotechnol.* **2018**, *14* (12), 2102–2113. https://doi.org/10.1166/jbn.2018.2624.
17. Guo, H.; Li, F.; Xu, W.; Chen, J.; Hou, Y.; Wang, C.; Ding, J.; Chen, X. Mucoadhesive Cationic Polypeptide Nanogel with Enhanced Penetration for Efficient Intravesical Chemotherapy of Bladder Cancer. *Adv. Sci.* **2018**, *5* (6), 1800004. https://doi.org/10.1002/advs.201800004.
18. Zhang, Y.; Wang, F.; Li, M.; Yu, Z.; Qi, R.; Ding, J.; Zhang, Z.; Chen, X. Self-Stabilized Hyaluronate Nanogel for Intracellular Codelivery of Doxorubicin and Cisplatin to Osteosarcoma. *Adv. Sci.* **2018**, *5* (5), 1700821. https://doi.org/10.1002/advs.201700821.
19. Luo, L.; Zhu, C.; Yin, H.; Jiang, M.; Zhang, J.; Qin, B.; Luo, Z.; Yuan, X.; Yang, J.; Li, W.; Du, Y.; You, J. Laser Immunotherapy in Combination with Perdurable PD-1 Blocking for the Treatment of Metastatic Tumors. *ACS Nano* **2018**, *12* (8), 7647–7662. https://doi.org/10.1021/acsnano.8b00204.
20. Nam, J.; Son, S.; Ochyl, L. J.; Kuai, R.; Schwendeman, A.; Moon, J. J. Chemo-photothermal therapy combination elicits anti-tumor immunity against advanced metastatic cancer. *Nat. Commun.* **2018,** *9* (1), 1074. https://doi.org/10.1038/s41467-018-03473-9.
21. Wang, C.; Ye, Y.; Hu, Q.; Bellotti, A.; Gu, Z. Tailoring Biomaterials for Cancer Immunotherapy: Emerging Trends and Future Outlook. *Adv. Mater*. **2017**, *29* (29). https://doi.org/10.1002/adma.201606036.
22. Stead, S. O.; Kireta, S.; McInnes, S. J. P.; Kette, F. D.; Sivanathan, K. N.; Kim, J.; Cueto-Diaz, E. J.; Cunin, F.; Durand, J. O.; Drogemuller, C. J.; Carroll, R. P.; Voelcker, N. H.; Coates, P. T. Murine and Non-Human Primate Dendritic Cell Targeting Nanoparticles for in Vivo Generation of Regulatory T-Cells. *ACS Nano* **2018**, *12* (7), 6637–6647. https://doi.org/10.1021/acsnano.8b01625.
23. Yang, R.; Xu, J.; Xu, L.; Sun, X.; Chen, Q.; Zhao, Y.; Peng, R.; Liu, Z. Cancer Cell Membrane-Coated Adjuvant Nanoparticles with Mannose Modification for Effective Anticancer Vaccination. *ACS Nano* **2018**, *12* (6), 5121–5129. https://doi.org/10.1021/acsnano.7b09041.
24. Yang, M.; Ding, J.; Feng, X.; Chang, F.; Wang, Y.; Gao, Z.; Zhuang, X.; Chen, X. Scavenger Receptor-Mediated Targeted Treatment of Collagen-Induced Arthritis by Dextran Sulfate-Methotrexate Prodrug. *Theranostics* **2017**, *7* (1), 97–105. https://doi.org/10.7150/thno.16844.
25. Bahmani, B.; Uehara, M.; Jiang, L.; Ordikhani, F.; Banouni, N.; Ichimura, T.; Solhjou, Z.; Furtmüller, G. J.; Brandacher, G.; Alvarez, D.; von Andrian, U. H.; Uchimura, K.; Xu Q.; Vohra, I.; Yilmam, O. A.; Haik, Y.; Azzi, J.; Kasinath, V.; Bromberg, J. S.; McGrath, M. M.; Abdi, R. Targeted delivery of immune therapeutics to lymph nodes prolongs cardiac allograft survival. *J. Clin. Invest.* **2018**, *128* (11), 4770–4786. https://doi.org/10.1172/JCI120923.
26. Ou, W.; Thapa, R. K.; Jiang, L.; Soe, Z. C.; Gautam, M.; Chang, J. H.; Jeong, J. H.; Ku, S. K.; Choi, H. G.; Yong, C. S.; Kim, J. O. Regulatory T cell-targeted hybrid nanoparticles combined with immuno-checkpoint blockage for cancer immunotherapy. *J. Controlled Release* **2018**, *281*, 84–96. https://doi.org/10.1016/j.jconrel.2018.05.018.
27. Heo, R.; You, D. G.; Um, W.; Choi, K. Y.; Jeon, S.; Park, J. S.; Choi, Y.; Kwon, S.; Kim, K.; Kwon, I. C.; Jo, D. G.; Kang, Y. M.; Park, J. H. Dextran sulfate nanoparticles as a theranostic nanomedicine for rheumatoid arthritis. *Biomaterials* **2017**, *131*, 15–26. https://doi.org/10.1016/j.biomaterials.2017.03.044.
28. Jiang, Z.; Chen, J.; Cui, L.; Zhuang, X.; Ding, J.; Chen, X. Advances in Stimuli-Responsive Polypeptide Nanogels. *Small Methods* **2018***, 2* (3), 1700307 https://doi.org/10.1002/smtd.201700307.
29. Ding, J.; Feng, X.; Jiang, Z.; Xu, W.; Guo, H.; Zhuang, X.; Chen, X. Polymer-Mediated Penetration-Independent Cancer Therapy. *Biomacromolecules* **2019**, *20* (12), 4258–4271. https://doi.org/10.1021/acs.biomac.9b01263.
30. Li, D.; Han, J.; Ding, J.; Chen, L.; Chen, X. Acid-sensitive dextran prodrug: A higher molecular weight makes a better efficacy. *Carbohydr. Polym*. **2017**, *161*, 33–41. https://doi.org/10.1016/j.carbpol.2016.12.070.
31. Feng, X.; Li, D.; Han, J.; Zhuang, X.; Ding, J. Schiff base bond-linked polysaccharide–doxorubicin conjugate for upregulated cancer therapy. *Materials Science and Engineering: C* **2017,** *76*, 1121–1128. https://doi.org/10.1016/j.msec.2017.03.201.
32. Zhang, C.; Shi, G.; Zhang, J.; Song, H.; Niu, J.; Shi, S.; Huang, P.; Wang, Y.; Wang, W.; Li, C.; Kong, D. Targeted antigen delivery to dendritic cell via functionalized alginate nanoparticles for cancer immunotherapy. *J. Controlled Release* **2017**, *256*, 170–181. https://doi.org/10.1016/j.jconrel.2017.04.020.
33. Cheng, K.; Ding, Y.; Zhao, Y.; Ye, S.; Zhao, X.; Zhang, Y.; Ji, T.; Wu, H.; Wang, B.; Anderson, G. J.; Ren, L.; Nie, G. Sequentially Responsive Therapeutic Peptide Assembling Nanoparticles for Dual-Targeted Cancer Immunotherapy. *Nano Lett.* **2018**, *18* (5), 3250–3258. https://doi.org/10.1021/acs.nanolett.8b01071.
34. Li, D.; Zhang, G.; Xu, W.; Wang, J.; Wang, Y.; Qiu, L.; Ding, J.; Yang, X. Investigating the Effect of Chemical Structure of Semiconducting Polymer Nanoparticle on Photothermal Therapy and Photoacoustic Imaging. *Theranostics* **2017**, *7* (16), 4029–4040. https://doi.org/10.7150/thno.19538.
35. Madan, R. A.; Turkbey, B.; Lepone, L. M.; Donahue, R. N.; Grenga, I.; Borofsky, S.; Pinto, P. A.; Citrin, D. E.; Kaushal, A.; Krauze, A. V.; McMahon, S.; Rauchhorst, M.; Couvillon, A.; Falk, M. H.; Eggleton, P.; Choyke, P. L.; Dahut, W. L.; Schlom, J.; Gulley, J. Changes in

multiparametric prostate MRI and immune subsets in patients (Pts) receiving neoadjuvant immunotherapy and androgen deprivation therapy (ADT) prior to radiation. *J. Clin. Oncol.* **2017**, *35* (6_suppl), 30–30. https://doi.org/10.1200/JCO.2017.35.6_suppl.30.

36. Oyen, D.; Torres, J. L.; Wille-Reece, U.; Ockenhouse, C. F.; Emerling, D.; Glanville, J.; Volkmuth, W.; Flores-Garcia, Y.; Zavala, F.; Ward, A. B.; King, C. R.; Wilson, I. A. Structural basis for antibody recognition of the NANP repeats in *Plasmodium falciparum* circumsporozoite protein. *Proc. Natl. Acad. Sci. U. S. A.* **2017**, *114* (48), E10438–E10445. https://doi.org/10.1073/pnas.1715812114.
37. Witte, D.; Cunliffe, N. A.; Turner, A. M.; Ngulube, E.; Ofori-Anyinam, O.; Vekemans, J.; Chimpeni, Ph.; Lievens, M.; Wilson, T. P.; Njiram'madzi, J.; Mendoza, Y. G.; Leach, A. Safety and Immunogenicity of Seven Dosing Regimens of the Candidate RTS,S/AS01$_E$ Malaria Vaccine Integrated Within an Expanded Program on Immunization Regimen. A Phase II, Single-Center, Open, Controlled Trial in Infants in Malawi. *The Pediatric Infectious Disease Journal* **2018**, *37* (5), 483–491. https://doi.org/10.1097/INF.0000000000001937.
38. Dang, B. N.; Kwon, T. K.; Lee, S.; Jeong, J. H.; Yook, S. Nanoparticle-based immunoengineering strategies for enhancing cancer immunotherapy. *J. Controlled Release* **2024**, *365*, 773–800. https://doi.org/10.1016/j.jconrel.2023.12.007.
39. Feng, B.; Zhou, F.; Hou, B.; Wang, D.; Wang, T.; Fu, Y.; Ma, Y.; Yu, H.; Li, Y. Binary Cooperative Prodrug Nanoparticles Improve Immunotherapy by Synergistically Modulating Immune Tumor Microenvironment. *Adv. Mater.* **2018**, *30* (38), e1803001. https://doi.org/10.1002/adma.201803001.
40. Fesnak, A. D.; June, C. H.; Levine, B. L. Engineered T cells: the promise and challenges of cancer immunotherapy. *Nat. Rev. Cancer* **2016**, *16* (9), 566–581. https://doi.org/10.1038/nrc.2016.97.
41. Zhang, Q.; Wei, W.; Wang, P.; Zuo, L.; Li, F.; Xu, J.; Xi, X.; Gao, X.; Ma, G.; Xie, H. Y. Biomimetic Magnetosomes as Versatile Artificial Antigen-Presenting Cells to Potentiate T-Cell-Based Anticancer Therapy. *ACS Nano* **2017**, *11* (11), 10724–10732. https://doi.org/10.1021/acsnano.7b04955.
42. Chiang, C. S.; Lin, Y. J.; Lee, R.; Lai, Y. H.; Cheng, H. W.; Hsieh, C. H.; Shyu, W. C.; Chen, S. Y. Combination of fucoidan-based magnetic nanoparticles and immunomodulators enhances tumour-localized immunotherapy. *Nat. Nanotechnol.* **2018**, *13* (8), 746–754. https://doi.org/10.1038/s41565-018-0146-7.
43. Sun, Q.; Zhou, Z.; Qiu, N.; Shen, Y. Rational Design of Cancer Nanomedicine: Nanoproperty Integration and Synchronization. *Adv. Mater.* **2017**, *29* (14). https://doi.org/10.1002/adma.201606628.
44. Qiu, F.; Becker, K. W.; Knight, F. C.; Baljon, J. J.; Sevimli, S.; Shae, D.; Gilchuk P.; Joyce, S.; Wilson, J. T. Poly(propylacrylic acid)-peptide nanoplexes as a platform for enhancing the immunogenicity of neoantigen cancer vaccines. *Biomaterials* **2018**, *182*, 82–91. https://doi.org/10.1016/j.biomaterials.2018.07.052.
45. Jabulowsky, R. A.; Loquai, C.; Derhovanessian, E.; Grabbe, S.; Türeci, Ö.; Sahin, U. A first-in-human phase I/II clinical trial assessing novel mRNA-lipoplex nanoparticles encoding shared tumor antigens for immunotherapy of malignant melanoma. *Ann. Oncol.* **2018**, *29*, VIII439. https://doi.org/10.1093/annonc/mdy288.109.
46. Zhao, J.; Yang, H.; Li, J.; Wang, Y.; Wang, X. Fabrication of pH-responsive PLGA(UCNPs/DOX) nanocapsules with upconversion luminescence for drug delivery. *Scientific reports* **2017**, *7* (1), 18014. https://doi.org/10.1038/s41598-017-16948-4.
47. Cohen, A. D.; Lendvai, N.; Nataraj, S.; Imai, N.; Jungbluth, A. A.; Tsakos, I.; Rahman, A.; Mei, A. H.; Singh, H.; Zarychta, K.; Kim-Schulze, S.; Park, A.; Venhaus, R.; Alpaugh, K.; Gnjatic, S.; Cho, H. J. Autologous Lymphocyte Infusion Supports Tumor Antigen Vaccine-Induced Immunity in Autologous Stem Cell Transplant for Multiple Myeloma. *Cancer Immunol. Res.* **2019**, *7* (4), 658–669. https://doi.org/10.1158/2326-6066.CIR-18-0198.
48. Dreno, B.; Thompson, J. F.; Smithers, B. M.; Santinami, M.; Jouary, T.; Gutzmer, R.; Levchenko, E.; Rutkowski, P.; Grob, J. J.; Korovin, S.; Drucis, K.; Grange, F.; Machet, L.; Hersey, P.; Krajsova, I.; Testori, A.; Conry, R.; Guillot, B.; Kruit, W. H. J.; Demidov, L.; Thompson, J. A.; Bondarenko, I.; Jaroszek, J.; Puig, S.; Cinat, G.; Hauschild, A.; Goeman, J. J.; van Houwelingen, H. C.; Ulloa-Montoya, F.; Callegaro, A.; Dizier, B.; Spiessens, B.; Debois, M.; Brichard, V. G.; Louahed, J.; Therasse, P.; Debruyne, C.; Kirkwood, J. M. MAGE-A3 immunotherapeutic as adjuvant therapy for patients with resected, MAGE-A3-positive, stage III melanoma (DERMA): a double-blind, randomised, placebo-controlled, phase 3 trial. *Lancet Oncol.* **2018**, *19* (7), 916–929. https://doi.org/10.1016/S1470-2045(18)30254-7.
49. McQuade, J. L.; Homsi, J.; Torres-Cabala, C. A.; Bassett, R.; Popuri, R. M.; James, M. L.; Vence, L. M.; Hwu, W. J. A phase II trial of recombinant MAGE-A3 protein with immunostimulant AS15 in combination with high-dose Interleukin-2 (HDIL2) induction therapy in metastatic melanoma. *BMC Cancer* **2018**, *18* (1), 1274. https://doi.org/10.1186/s12885-018-5193-9.
50. Kosmides, A. K.; Meyer, R. A.; Hickey, J. W.; Aje, K.; Cheung, K. N.; Green, J. J.; Schneck, J. P. Biomimetic biodegradable artificial antigen presenting cells synergize with PD-1 blockade to treat melanoma. *Biomaterials* **2017**, *118*, 16–26. https://doi.org/10.1016/j.biomaterials.2016.11.038.
51. Min, Y.; Roche, K. C.; Tian, S.; Eblan, M. J.; McKinnon, K. P.; Caster, J. M.; Chai, S.; Herring, L. E.; Zhang, L.; Zhang, T.; DeSimone, J. M.; Tepper, J. E.; Vincent, B. G.; Serody, J. S.; Wang, A. Z. Antigen-capturing nanoparticles improve the abscopal effect and cancer immunotherapy. *Nat. Nanotechnol*. **2017**, *12* (9), 877–882. https://doi.org/10.1038/nnano.2017.113.
52. Zheng, D. W.; Chen, J. L.; Zhu, J. Y.; Rong, L.; Li, B.; Lei, Q.; Fan, J. X.; Zou, M. Z.; Li, C.; Cheng, S. X.; Xu, Z.; Zhang, X. Z. Highly Integrated Nano-Platform for Breaking the Barrier between Chemotherapy and Immunotherapy. *Nano Lett*. **2016**, *16* (7), 4341–4347. https://doi.org/10.1021/acs.nanolett.6b01432.
53. Velpurisiva, P.; Gad, A.; Piel, B.; Jadia, R.; Rai, P. Nanoparticle Design Strategies for Effective Cancer Immunotherapy. *Journal of Biomedicine* **2017**, *2*, 64–77. https://doi.org/10.7150/jbm.18877.
54. Viswanath, D.; Park, J.; Misra, R.; Pizzuti, V. J.; Shin, S.-H.; Doh, J.; Won, Y.-Y. Nanotechnology-enhanced radiotherapy and the abscopal effect: Current status and challenges of nanomaterial-based radio-immunotherapy. *Wiley Interdiscip. Rev.: Nanomed. Nanobiotechnol.* **2024**, *16* (1), e1924. https://doi.org/10.1002/wnan.1924.
55. Song, W.; Shen, L.; Wang, Y.; Liu, Q.; Goodwin, T. J.; Li, J.; Dorosheva, O.; Liu, T.; Liu, R.; Huang, L. Synergistic and low adverse effect cancer immunotherapy by immunogenic chemotherapy and locally expressed PD-L1 trap. *Nat. Commun.* **2018**, *9* (1), 2237. https://doi.org/10.1038/s41467-018-04605-x.
56. Tang, W.; Yang, J.; Yuan, Y.; Zhao, Z.; Lian, Z.; Liang, G. Paclitaxel nanoparticle awakens immune system to fight against cancer. *Nanoscale* **2017**, *9* (19), 6529–6536. https://doi.org/10.1039/c6nr09895a.
57. Draz, M. S.; Wang, Y.-J.; Chen, F. F.; Xu, Y.; Shafiee, H. Electrically Oscillating Plasmonic Nanoparticles for Enhanced DNA Vaccination against Hepatitis C Virus. *Adv. Funct. Mater.* **2017**, *27* (5), 1604139. https://doi.org/10.1002/adfm.201604139.
58. Dakterzada, F.; Mohabati Mobarez, A.; Habibi Roudkenar, M.; Mohsenifar, A. Induction of humoral immune response against Pseudomonas aeruginosa flagellin(1-161) using gold nanoparticles as an adjuvant. *Vaccine* **2016**, *34* (12), 1472–1479. https://doi.org/10.1016/j.vaccine.2016.01.041.
59. Vetro, M.; Safari, D.; Fallarini, S.; Salsabila, K.; Lahmann, M.; Penadés, S.; Lay, L.; Marradi, M.; Compostella, F. Preparation and immunogenicity of gold glyco-nanoparticles as antipneumococcal vaccine model. *Nanomedicine* **2017**, *12* (1), 13–23. https://doi.org/10.2217/nnm-2016-0306.

ISSN 2308-8303 (Print) / 2518-1548 (Online)

60. Chien-Wei Lin, L.; Chattopadhyay, S.; Lin, J.-C.; Hu, C.-M. J. Advances and Opportunities in Nanoparticle- and Nanomaterial-Based Vaccines against Bacterial Infections. *Adv. Healthcare Mater.* **2018**, *7* (13), 1701395. https://doi.org/10.1002/adhm.201701395.
61. Pavot, V.; Climent, N.; Rochereau, N.; Garcia, F.; Genin, C.; Tiraby, G.; Vernejoul, F.; Perouzel, E.; Lioux, T.; Verrier, B.; Paul, S. Directing vaccine immune responses to mucosa by nanosized particulate carriers encapsulating NOD ligands. *Biomaterials* **2016**, *75*, 327–339. https://doi.org/10.1016/j.biomaterials.2015.10.034.
62. Gargett, T.; Abbas, M. N.; Rolan, P.; Price, J. D.; Gosling, K. M.; Ferrante, A.; Ruszkiewicz, A.; Atmosukarto, I. I. C.; Altin, J.; Parish, C. R.; Brown, M. P. Phase I trial of Lipovaxin-MM, a novel dendritic cell-targeted liposomal vaccine for malignant melanoma. *Cancer Immunol. Immunother.* **2018**, *67* (9), 1461–1472. https://doi.org/10.1007/s00262-018-2207-z.
63. Pujol, J. L.; De Pas, T.; Rittmeyer, A.; Vallières, E.; Kubisa, B.; Levchenko, E.; Wiesemann, S.; Masters, G. A.; Shen, R.; Tjulandin, S. A.; Hofmann, H. S.; Vanhoutte, N.; Salaun, B.; Debois, M.; Jarnjak, S.; De Sousa Alves, P. M.; Louahed, J.; Brichard, V. G.; Lehmann, F. F. Safety and Immunogenicity of the PRAME Cancer Immunotherapeutic in Patients with Resected Non-Small Cell Lung Cancer: A Phase I Dose Escalation Study. *J. Thorac. Oncol*. **2016**, *11* (12), 2208–2217. https://doi.org/10.1016/j.jtho.2016.08.120.
64. Zhu, G.; Zhang, F.; Ni, Q.; Niu, G.; Chen, X. Efficient Nanovaccine Delivery in Cancer Immunotherapy. *ACS Nano* **2017**, *11* (3), 2387–2392. https://doi.org/10.1021/acsnano.7b00978.

Information about the authors:
Oleksandr F. Piminov, D.Sci. in Pharmacy, Professor, Director of the Institute for Advanced Training of Pharmacy Specialists of the National University of Pharmacy of the Ministry of Health of Ukraine; https://orcid.org/0000-0003-4369-907X.
Rita V. Sahaidak-Nikitiuk (*corresponding author*), D.Sci. in Pharmacy, Professor, Head of the Department of Pharmaceutical Technology, Standardization and Certification of Drugs, Institute for Advanced Training of Pharmacy Specialists of the National University of Pharmacy of the Ministry of Health of Ukraine; https://orcid.org/0000-0002-9337-7741; e-mail for correspondence: sagaidak_rita@ukr.net; tel. +380667899940.
Anna I. Kvitchata, Ph.D. in Medicine, Associate Professor of the Department of Clinical Pharmacology, Institute for Advanced Training of Pharmacy Specialists of the National University of Pharmacy of the Ministry of Health of Ukraine; https://orcid.org/0000-0001-8093-2569.
Svitlana M. Rolik-Attia, Ph.D. in Pharmacy, Associate Professor of the Department of Pharmaceutical Technology, Standardization and Certification of Drugs, Institute for Advanced Training of Pharmacy Specialists of the National University of Pharmacy of the Ministry of Health of Ukraine; https://orcid.org/0000-0002-0299-5895.