Middle Eastern Cancer and Oncology Journal (MECOJ)
ISSN: 3080-1427 (online) / 3080-1419 (print)
Volume 1, Issue 2 (April 2025 – June 2025), pp: 8-12

Mini-Review

Cancer Vaccines: Breakthroughs, Challenges, and Future Perspectives in Oncology

Startsev V. Yu [1,*]

[1] St. Petersburg State Pediatric Medical University, St. Petersburg, Russian Federation.

E-mail: doc.urolog@gmail.com [1,*]

Received: 04 February 2025 | Revised: 05 March 2025 | Accepted: 10 April 2025 | Published: 18 April 2025

Abstract

Cancer continues to pose a significant global health burden, accounting for millions of cases and fatalities each year. Conventional therapeutic modalities, including surgery, chemotherapy, and radiotherapy, have yielded improved outcomes. However, their limitations and adverse effects underscore the imperative for novel therapeutic strategies, such as cancer vaccines. These vaccines, grounded in immunotherapeutic principles, have been shown to activate the immune system, thereby inducing tumor-specific responses. This mini-review explores the immunological foundations, classifications, and current limitations of cancer vaccines, with emphasis on peptide-based, recombinant, cell-based, and nucleic acid-based modalities. The manuscript also examines the significance of neoantigen identification and the tumor microenvironment in determining vaccine effectiveness. Notwithstanding noteworthy advancements, challenges such as immune evasion, low mutation rates, and an immunosuppressive tumor milieu endure. The effective incorporation of cancer vaccines into standard oncological care is contingent upon future research and clinical breakthroughs.

Keywords: *Cancer Vaccines, Promises, Barriers, Types, Personalize Cancer Vaccine.*

*** Correspondence Author**

Cite This Article: Yu, S. v. (2025). Cancer Vaccines: Breakthroughs, Challenges, and Future Perspectives in Oncology. *Middle Eastern Cancer and Oncology Journal*, *1*(2), 8–12. https://doi.org/10.61706/MECOJ160132

Introduction

Cancer is a term that encompasses a broad spectrum of diseases marked by the abnormal growth and dissemination of malignant cells. Its recognition dates back to ancient civilizations, yet it remains a pressing challenge despite considerable progress in scientific understanding. Current therapeutic modalities, including surgery, radiotherapy, chemotherapy, and immunotherapy, have contributed to significant advancements in the field of care. Nevertheless, the persistent global impact of cancer emphasizes the urgency for better early detection techniques, more individualized treatment protocols, and improved patient outcomes (Srivastava et al., 2024).

According to global statistics, in the year 2020, approximately 19.3 million individuals were diagnosed with cancer for the first time, and approximately 10 million of those individuals died from the disease. These figures reflect the limitations of standard therapies, which, while often effective, can be associated with significant toxicity and restricted efficacy in certain contexts (T. Fan et al., 2023).

Advancements in the field of oncology have led to significant improvements in diagnostic accuracy and therapeutic strategies. These advancements are supported by various innovations, including genetic profiling, liquid biopsies, and advanced imaging technologies such as CT, MRI, and PET. Among the aforementioned developments, cancer vaccines have emerged as a promising avenue, offering both preventive and therapeutic potential, particularly in malignancies characterized by identifiable tumor-associated antigens, such as melanoma and prostate cancer (Kaczmarek et al., 2023; Sheikhlary et al., 2024; Srivastava et al., 2024).

Cancer Vaccines: Promises and Barriers

Vaccines have traditionally functioned as a primary defense against infectious diseases. However, significant advancements in the field of immunology have led to the extension of these mechanisms to the realm of cancer therapy and prevention. Initial efforts concentrated on the development of therapeutic cancer vaccines targeting tumor-associated antigens (TAAs) or self-antigens expressed by cancer cells. However, these approaches frequently proved ineffective in inducing robust and persistent T-cell responses. In contrast, emerging strategies employing neoantigen-based vaccines exhibit enhanced specificity by guiding the immune system towards antigens exclusively present in tumors. This approach serves to mitigate the risk of immune tolerance and unintended tissue damage (Sobhani et al., 2022).

A critical component of effective vaccine design lies in the identification and selection of neoantigens or neoepitopes, which are uniquely presented by tumor cells. In contrast to self-antigens, which are generally well-tolerated by the immune system, neoantigens derived from tumor-specific mutations have been demonstrated to elicit more robust immune responses. Indeed, T-cell reactivity to neoantigens can be significantly greater than to TAAs due to higher immunogenicity and a reduced likelihood of central or peripheral tolerance (Sobhani et al., 2022). However, several features of the tumor microenvironment, including hypoxia, nutrient scarcity, acidic pH, oxidative stress, and the presence of immunosuppressive elements such as regulatory T cells and myeloid-derived suppressor cells, have been shown to interfere with vaccine efficacy. Additional barriers to effective treatment include low tumor mutational burden, immune evasion mechanisms such as antigen loss, and impaired antigen presentation due to dysfunctional dendritic cells (Belli et al., 2018; Roma-Rodrigues et al., 2019; Vedenko et al., 2020).

Types of Cancer Vaccines

Peptide-Based Vaccines:

Peptide vaccines employ short antigenic sequences derived from tumor-associated or tumor-specific proteins to activate the immune system. These peptides primarily stimulate immune responses by engaging CD8+ cytotoxic and CD4+ helper T cells through their presentation on MHC class I and II molecules. These vaccines have been demonstrated to elicit both cellular and humoral immune responses, thereby contributing to long-term tumor surveillance. A notable illustration of this phenomenon is the FDA-approved therapeutic cancer vaccine known as sipuleucel-T (Provenge). This vaccine is notable for its application in cases of prostate cancer that has become resistant to castration, thereby demonstrating the clinical feasibility of this therapeutic approach (Abd-Aziz & Poh, 2022; Laumont & Perreault, 2018; Mizukoshi et al., 2022).

Recombinant Vaccines:

Recombinant cancer vaccines are made using genetically modified viruses or bacteria. These modified viruses or bacteria are designed to deliver tumor antigens. These vaccines can be classified into three categories: inactivated, live-attenuated, or subunit vaccines. They function by either directly presenting antigens through MHC pathways or indirectly by eliciting inflammatory signals from infected or lysed cells. This activates antigen-presenting cells (APCs). Vaccine engineering has seen significant improvements, with new developments in antigen presentation leading to stronger immune responses (Atkin-Smith et al., 2018; de Pinho Favaro et al., 2022; Y. Fan et al., 2021; Lauring et al., Mayer & Impens

(2021); Mendonça et al. (2021); MOREIN et al. (1978); Pardoll (1998); Pishesha et al. (2021); Pranchevicius & Vieira (2013); Ragothaman & Yoo (2023); Sanders et al. (2015); Toussaint et al. (2013); Travieso et al. (2022); Yoo et al. (2021).

Cell-Based Vaccines:

These vaccines use immune cells, like dendritic cells (DCs), or genetically engineered tumor cells to make the body fight the tumor. Dendritic cell vaccines work by presenting tumor antigens to T cells, which triggers a targeted immune response. Some types of DCs, like conventional (cDCs), plasmacytoid (pDCs), and monocyte-derived (moDCs), play a special role in immune system activation. They do this by producing cytokines and presenting antigens (Keenan & Jaffee, 2012).

Nucleic Acid-Based Immunization: DNA and mRNA Strategies

This category includes DNA and mRNA vaccines designed to introduce tumor antigen-encoding sequences into host cells to stimulate immunity.

DNA Vaccines: These vaccines use bacterial plasmids. Plasmids are pieces of DNA that can be used to make vaccines. They get into the cell nucleus and then become mRNA. Then, the mRNA is translated into antigenic proteins. The tumor antigens that result are then shown through MHC class I and II pathways. This activates both the adaptive and innate immune mechanisms.

mRNA Vaccines deliver synthetic messenger RNA directly to antigen-presenting cells (APCs), skipping the transcription step. After the body's cells absorb the mRNA, it is translated into antigenic proteins. These proteins are then processed and displayed to T cells. These vaccines can also help activate B cells and stimulate the production of antibodies. This makes them a strong option for immunotherapy (Cui, 2005; Del Prete et al., 2023; Jorritsma et al., 2016; Katakam et al., 2015; Liang et al., 2017; Lopes et al., 2019; Manh et al., 2013; Murphy & Murphy, 2022; Ni, 2023; Rojas et al., 2023; Stevenson et al., 2004; Wang et al., 2022).

Personalize Cancer Vaccine

Personalized cancer vaccines are made to recognize the unique tumor-specific mutations of each patient. By studying the genetic changes in tumors, researchers can develop vaccines that target these changes and help the body's immune system fight the cancer. This personalized approach makes the immune system better at detecting and destroying harmful cells. The way we make immunotherapy work for each patient's genetic tumor profile makes the treatment more precise and effective while reducing any immune responses that we don't want (Liu et al., 2022; Maman & Witz, 2018).

Conclusion

Cancer vaccines represent a significant advancement in the field of cancer therapy, offering a more precise and less toxic approach to treatment. By mobilizing the immune system to identify and attack tumor-specific antigens, these vaccines offer a promising complement to conventional treatments. However, the widespread adoption of these technologies is hindered by two major factors. Firstly, tumor-induced immune suppression presents a significant challenge, as it impedes the efficacy of immunotherapies. Secondly, the complexities of the tumor microenvironment contribute to the challenges associated with the adoption of these technologies. Continued advancements in areas such as neoantigen discovery, immunomodulatory tactics, and delivery platforms are essential for overcoming these barriers. Pursuant to sustained research and clinical innovation, cancer vaccines may soon play a central role in enhancing survival and quality of life for patients battling cancer worldwide.

References

Abd-Aziz, N., & Poh, C. L. (2022). Development of Peptide-Based Vaccines for Cancer. *Journal of Oncology*, *2022*, 1–17. https://doi.org/10.1155/2022/9749363

Atkin-Smith, G. K., Duan, M., Chen, W., & Poon, I. K. H. (2018). The induction and consequences of Influenza A virus-induced cell death. *Cell Death & Disease*, *9*(10), 1002. https://doi.org/10.1038/s41419-018-1035-6

Belli, C., Trapani, D., Viale, G., D'Amico, P., Duso, B. A., Della Vigna, P., Orsi, F., & Curigliano, G. (2018). Targeting the microenvironment in solid tumors. *Cancer Treatment Reviews*, *65*, 22–32. https://doi.org/10.1016/j.ctrv.2018.02.004

Cui, Z. (2005). *DNA Vaccine* (pp. 257–289). https://doi.org/10.1016/S0065-2660(05)54011-2

de Pinho Favaro, M. T., Atienza-Garriga, J., Martínez-Torró, C., Parladé, E., Vázquez, E., Corchero, J. L., Ferrer-Miralles, N., & Villaverde, A. (2022). Recombinant vaccines in 2022: a perspective from the cell factory. *Microbial Cell Factories*, *21*(1), 203. https://doi.org/10.1186/s12934-022-01929-8

Del Prete, A., Salvi, V., Soriani, A., Laffranchi, M., Sozio, F., Bosisio, D., & Sozzani, S. (2023). Dendritic cell subsets in cancer immunity and tumor antigen sensing. *Cellular & Molecular Immunology*, *20*(5), 432–447. https://doi.org/10.1038/s41423-023-00990-6

Fan, T., Zhang, M., Yang, J., Zhu, Z., Cao, W., & Dong, C. (2023). Therapeutic cancer vaccines:

advancements, challenges and prospects. *Signal Transduction and Targeted Therapy*, *8*(1), 450. https://doi.org/10.1038/s41392-023-01674-3

Fan, Y., Bai, T., Tian, Y., Zhou, B., Wang, Y., & Yang, L. (2021). H2O2-Inactivated Salmonella typhimurium RE88 Strain as a New Cancer Vaccine Carrier: Evaluation in a Mouse Model of Cancer. *Drug Design, Development and Therapy*, *Volume 15*, 209–222. https://doi.org/10.2147/DDDT.S282660

Jorritsma, S. H. T., Gowans, E. J., Grubor-Bauk, B., & Wijesundara, D. K. (2016). Delivery methods to increase cellular uptake and immunogenicity of DNA vaccines. *Vaccine*, *34*(46), 5488–5494. https://doi.org/10.1016/j.vaccine.2016.09.062

Kaczmarek, M., Poznańska, J., Fechner, F., Michalska, N., Paszkowska, S., Napierała, A., & Mackiewicz, A. (2023). Cancer Vaccine Therapeutics: Limitations and Effectiveness—A Literature Review. *Cells*, *12*(17), 2159. https://doi.org/10.3390/cells12172159

Katakam, A. K., Brightbill, H., Franci, C., Kung, C., Nunez, V., Jones, C., Peng, I., Jeet, S., Wu, L. C., Mellman, I., Delamarre, L., & Austin, C. D. (2015). Dendritic cells require NIK for CD40-dependent cross-priming of CD8+ T cells. *Proceedings of the National Academy of Sciences*, *112*(47), 14664–14669. https://doi.org/10.1073/pnas.1520627112

Keenan, B. P., & Jaffee, E. M. (2012). Whole Cell Vaccines—Past Progress and Future Strategies. *Seminars in Oncology*, *39*(3), 276–286. https://doi.org/10.1053/j.seminoncol.2012.02.007

Laumont, C. M., & Perreault, C. (2018). Exploiting non-canonical translation to identify new targets for T cell-based cancer immunotherapy. *Cellular and Molecular Life Sciences*, *75*(4), 607–621. https://doi.org/10.1007/s00018-017-2628-4

Lauring, A. S., Jones, J. O., & Andino, R. (2010). Rationalizing the development of live attenuated virus vaccines. *Nature Biotechnology*, *28*(6), 573–579. https://doi.org/10.1038/nbt.1635

Liang, F., Lindgren, G., Lin, A., Thompson, E. A., Ols, S., Röhss, J., John, S., Hassett, K., Yuzhakov, O., Bahl, K., Brito, L. A., Salter, H., Ciaramella, G., & Loré, K. (2017). Efficient Targeting and Activation of Antigen-Presenting Cells In Vivo after Modified mRNA Vaccine Administration in Rhesus Macaques. *Molecular Therapy*, *25*(12), 2635–2647. https://doi.org/10.1016/j.ymthe.2017.08.006

Liu, J., Fu, M., Wang, M., Wan, D., Wei, Y., & Wei, X. (2022). Cancer vaccines as promising immuno-therapeutics: platforms and current progress. *Journal of Hematology & Oncology*, *15*(1), 28. https://doi.org/10.1186/s13045-022-01247-x

Lopes, A., Vandermeulen, G., & Préat, V. (2019). Cancer DNA vaccines: current preclinical and clinical developments and future perspectives. *Journal of Experimental & Clinical Cancer Research*, *38*(1), 146. https://doi.org/10.1186/s13046-019-1154-7

Maman, S., & Witz, I. P. (2018). A history of exploring cancer in context. *Nature Reviews Cancer*, *18*(6), 359–376. https://doi.org/10.1038/s41568-018-0006-7

Manh, T. V., Alexandre, Y., Baranek, T., Crozat, K., & Dalod, M. (2013). Plasmacytoid, conventional, and monocyte-derived dendritic cells undergo a profound and convergent genetic reprogramming during their maturation. *European Journal of Immunology*, *43*(7), 1706–1715. https://doi.org/10.1002/eji.201243106

Mayer, R. L., & Impens, F. (2021). Immunopeptidomics for next-generation bacterial vaccine development. *Trends in Microbiology*, *29*(11), 1034–1045. https://doi.org/10.1016/j.tim.2021.04.010

Mendonça, S. A., Lorincz, R., Boucher, P., & Curiel, D. T. (2021). Adenoviral vector vaccine platforms in the SARS-CoV-2 pandemic. *Npj Vaccines*, *6*(1), 97. https://doi.org/10.1038/s41541-021-00356-x

Mizukoshi, E., Nakagawa, H., Tamai, T., Kitahara, M., Fushimi, K., Nio, K., Terashima, T., Iida, N., Arai, K., Yamashita, T., Yamashita, T., Sakai, Y., Honda, M., & Kaneko, S. (2022). Peptide vaccine-treated, long-term surviving cancer patients harbor self-renewing tumor-specific CD8+ T cells. *Nature Communications*, *13*(1), 3123. https://doi.org/10.1038/s41467-022-30861-z

MOREIN, B., HELENIUS, A., SIMONS, K., PETTERSSON, R., KÄÄRIÄINEN, L., & SCHIRRMACHER, V. (1978). Effective subunit vaccines against an enveloped animal virus. *Nature*, *276*(5689), 715–718. https://doi.org/10.1038/276715a0

Murphy, T. L., & Murphy, K. M. (2022). Dendritic cells in cancer immunology. *Cellular & Molecular Immunology*, *19*(1), 3–13. https://doi.org/10.1038/s41423-021-00741-5

Ni, L. (2023). Advances in mRNA-Based Cancer Vaccines. *Vaccines*, *11*(10), 1599. https://doi.org/10.3390/vaccines11101599

Pardoll, D. M. (1998). Cancer vaccines. *Nature Medicine*, *4*(S5), 525–531. https://doi.org/10.1038/nm0598supp-525

Pishesha, N., Harmand, T. J., Rothlauf, P. W., Praest, P., Alexander, R. K., van den Doel, R., Liebeskind, M. J., Vakaki, M. A., McCaul, N., Wijne, C., Verhaar, E., Pinney, W., Heston, H., Bloyet, L.-M., Pontelli, M. C., Ilagan, Ma. X. G., Jan Lebbink, R., Buchser, W. J., Wiertz, E. J. H. J., … Ploegh, H. L.

(2021). A class II MHC-targeted vaccine elicits immunity against SARS-CoV-2 and its variants. *Proceedings of the National Academy of Sciences*, *118*(44). https://doi.org/10.1073/pnas.2116147118

Pranchevicius, M.-C. S., & Vieira, T. R. (2013). Production of recombinant immunotherapeutics for anticancer treatment. *Bioengineered*, *4*(5), 305–312. https://doi.org/10.4161/bioe.24666

Ragothaman, M., & Yoo, S. Y. (2023). Engineered Phage-Based Cancer Vaccines: Current Advances and Future Directions. *Vaccines*, *11*(5), 919. https://doi.org/10.3390/vaccines11050919

Rojas, L. A., Sethna, Z., Soares, K. C., Olcese, C., Pang, N., Patterson, E., Lihm, J., Ceglia, N., Guasp, P., Chu, A., Yu, R., Chandra, A. K., Waters, T., Ruan, J., Amisaki, M., Zebboudj, A., Odgerel, Z., Payne, G., Derhovanessian, E., … Balachandran, V. P. (2023). Personalized RNA neoantigen vaccines stimulate T cells in pancreatic cancer. *Nature*, *618*(7963), 144–150. https://doi.org/10.1038/s41586-023-06063-y

Roma-Rodrigues, C., Mendes, R., Baptista, P. V., & Fernandes, A. R. (2019). Targeting Tumor Microenvironment for Cancer Therapy. *International Journal of Molecular Sciences*, *20*(4), 840. https://doi.org/10.3390/ijms20040840

Sanders, B., Koldijk, M., & Schuitemaker, H. (2015). Inactivated Viral Vaccines. In *Vaccine Analysis: Strategies, Principles, and Control* (pp. 45–80). Springer Berlin Heidelberg. https://doi.org/10.1007/978-3-662-45024-6_2

Sheikhlary, S., Lopez, D. H., Moghimi, S., & Sun, B. (2024). Recent Findings on Therapeutic Cancer Vaccines: An Updated Review. *Biomolecules*, *14*(4), 503. https://doi.org/10.3390/biom14040503

Sobhani, N., Scaggiante, B., Morris, R., Chai, D., Catalano, M., Tardiel-Cyril, D. R., Neeli, P., Roviello, G., Mondani, G., & Li, Y. (2022). Therapeutic cancer vaccines: From biological mechanisms and engineering to ongoing clinical trials. *Cancer Treatment Reviews*, *109*, 102429. https://doi.org/10.1016/j.ctrv.2022.102429

Srivastava, S., Singh, D., Verma, S. K., Pandey, M., Sharma, A., Pandey, H., & Mishra, A. (2024). Recent advancements in cancer vaccines: A systematic review. *Vacunas*, *25*(1), 97–108. https://doi.org/10.1016/j.vacun.2023.10.005

Stevenson, F. K., Ottensmeier, C. H., Johnson, P., Zhu, D., Buchan, S. L., McCann, K. J., Roddick, J. S., King, A. T., McNicholl, F., Savelyeva, N., & Rice, J. (2004). DNA vaccines to attack cancer. *Proceedings of the National Academy of Sciences*, *101*(suppl_2), 14646–14652. https://doi.org/10.1073/pnas.0404896101

Toussaint, B., Chauchet, X., Wang, Y., Polack, B., & Gouëllec, A. Le. (2013). Live-attenuated bacteria as a cancer vaccine vector. *Expert Review of Vaccines*, *12*(10), 1139–1154. https://doi.org/10.1586/14760584.2013.836914

Travieso, T., Li, J., Mahesh, S., Mello, J. D. F. R. E., & Blasi, M. (2022). The use of viral vectors in vaccine development. *Npj Vaccines*, *7*(1), 75. https://doi.org/10.1038/s41541-022-00503-y

Vedenko, A., Panara, K., Goldstein, G., Ramasamy, R., & Arora, H. (2020). *Tumor Microenvironment and Nitric Oxide: Concepts and Mechanisms* (pp. 143–158). https://doi.org/10.1007/978-3-030-50224-9_10

Wang, Y., Zhang, R., Tang, L., & Yang, L. (2022). Nonviral Delivery Systems of mRNA Vaccines for Cancer Gene Therapy. *Pharmaceutics*, *14*(3), 512. https://doi.org/10.3390/pharmaceutics14030512

Yoo, J.-S., Sasaki, M., Cho, S. X., Kasuga, Y., Zhu, B., Ouda, R., Orba, Y., de Figueiredo, P., Sawa, H., & Kobayashi, K. S. (2021). SARS-CoV-2 inhibits induction of the MHC class I pathway by targeting the STAT1-IRF1-NLRC5 axis. *Nature Communications*, *12*(1), 6602. https://doi.org/10.1038/s41467-021-26910-8