

Personalized mRNA Cancer Vaccines: Advancing Precision Oncology Through Neoantigen-Directed Immunotherapy

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ABSTRACT

Cancer remains one of the leading causes of mortality worldwide despite significant advances in diagnosis and treatment. The emergence of personalized messenger RNA (mRNA)-based cancer vaccines has introduced a novel therapeutic strategy capable of integrating genomic medicine, immunology, and biotechnology into precision oncology. The objective of this review was to analyze the current scientific evidence regarding the biological foundations, immunological mechanisms, clinical applications, advantages, limitations, and future perspectives of personalized mRNA cancer vaccines. A scientific method-based narrative review methodology was employed through a structured search of peer-reviewed literature indexed in PubMed, Scopus, Web of Science, ScienceDirect, SpringerLink, and other internationally recognized databases. The evidence demonstrated that personalized mRNA vaccines can encode patient-specific neoantigens, stimulate robust CD4+ and CD8+ T-cell responses, enhance dendritic-cell-

mediated antigen presentation, and promote durable immunological memory. Clinical investigations have reported encouraging results in melanoma, pancreatic cancer, glioblastoma, lung cancer, and other malignancies, particularly when vaccines are combined with immune checkpoint inhibitors. The findings also revealed important advantages, including high therapeutic specificity, individualized treatment design, and rapid development capacity. However, challenges related to neoantigen selection, manufacturing costs, regulatory complexity, and healthcare infrastructure remain significant barriers to widespread implementation. From a regional perspective, countries such as Mexico, Colombia, and Ecuador are progressively expanding precision oncology capabilities, although important limitations persist regarding access to genomic technologies and advanced immunotherapies. Overall, personalized mRNA cancer vaccines represent a promising innovation with the potential to transform future cancer treatment through highly individualized and immune-based therapeutic approaches.

KEYWORDS

Personalized mRNA vaccines, Cancer immunotherapy, Precision oncology, Neoantigens, Messenger RNA, Cancer vaccines, Tumor immunology, Genomic medicine, Immune checkpoint inhibitors, Personalized medicine, Biotechnology, Translatio

INTRODUCTION

Cancer remains one of the leading causes of morbidity and mortality worldwide, representing a major challenge for healthcare systems, researchers, and policymakers. Despite substantial advances in surgery, radiotherapy, chemotherapy, targeted therapies, and immune checkpoint inhibitors, many malignant tumors continue to exhibit high rates of recurrence, therapeutic resistance, and disease progression. According to recent global estimates, cancer accounts for millions of new diagnoses and deaths annually, emphasizing the urgent need for innovative therapeutic approaches capable of providing more precise, durable, and personalized antitumor responses [1]. The emergence of precision oncology has transformed the management of cancer by promoting treatment strategies tailored to the molecular and immunological characteristics of individual patients, thereby improving therapeutic efficacy while reducing unnecessary toxicity [2].

Among the most promising developments in modern oncology is the application of messenger RNA (mRNA)-based vaccines for cancer treatment. Although mRNA technology gained worldwide recognition during the COVID-19 pandemic, its scientific foundations had been under development for several decades. Advances in RNA stabilization, nucleoside modification, lipid nanoparticle delivery systems, and genomic sequencing have enabled the translation of mRNA technology into personalized therapeutic platforms capable of targeting tumor-specific antigens with unprecedented precision [3,4]. Unlike conventional vaccines designed primarily for infectious disease prevention, therapeutic cancer vaccines seek to stimulate robust cellular immune responses against malignant cells by presenting tumor-associated antigens or patient-specific neoantigens to the immune system [5].

The concept of personalized cancer vaccination is based on the identification of unique genetic mutations within an individual tumor. These mutations can generate neoantigens, which are novel peptides absent from normal tissues and therefore highly recognizable by the immune system. Advances in next-generation sequencing and bioinformatics have facilitated the rapid identification of these neoantigens, enabling the development of individualized mRNA vaccines tailored to each patient's tumor profile [6]. Such vaccines can induce potent activation of CD4⁺ and CD8⁺ T lymphocytes, promote immunological memory, and enhance antitumor surveillance, making them particularly attractive as complementary therapies in precision oncology [7].

Recent clinical studies have demonstrated encouraging results regarding the safety, immunogenicity, and therapeutic potential of personalized mRNA vaccines. Landmark investigations in melanoma showed that individualized

neoantigen vaccines could generate broad and sustained T-cell responses while reducing the risk of disease recurrence [8,9]. Similarly, studies involving glioblastoma and pancreatic ductal adenocarcinoma have revealed that personalized mRNA vaccines can stimulate tumor-specific immune responses even in highly immunosuppressive tumor microenvironments [10,11]. The combination of mRNA vaccines with immune checkpoint inhibitors has attracted particular interest, as evidence suggests synergistic effects capable of enhancing antitumor immunity and improving clinical outcomes [12].

The success of mRNA vaccine platforms can be attributed to several biological and technological advantages. Unlike peptide-based or dendritic-cell vaccines, mRNA vaccines can be rapidly designed and manufactured, allowing adaptation to individual tumor mutational profiles. Furthermore, mRNA molecules do not integrate into the host genome, reducing concerns regarding insertional mutagenesis. Their transient expression profile, coupled with the ability to encode multiple neoantigens simultaneously, offers considerable flexibility for personalized therapeutic interventions [13]. Advances in lipid nanoparticle technology have also improved intracellular delivery, antigen presentation efficiency, and vaccine stability, overcoming many limitations previously associated with nucleic acid therapeutics [14].

Nevertheless, important challenges remain before personalized mRNA cancer vaccines can achieve widespread clinical implementation. The identification of clinically relevant neoantigens, variability in patient immune responses, manufacturing costs, regulatory requirements, and logistical complexities continue to limit accessibility in many healthcare systems [15]. Moreover, the heterogeneity of tumor biology and the immunosuppressive mechanisms present within the tumor microenvironment may influence vaccine effectiveness, requiring further optimization of vaccine design and combination strategies [16]. Long-term efficacy data are still emerging, and additional studies are necessary to determine the most effective clinical settings for vaccine administration across different cancer types and stages.

These challenges are particularly relevant in low- and middle-income regions, including Latin America, where disparities in access to genomic technologies, molecular diagnostics, immunotherapy, and specialized oncology services remain significant. Countries such as Mexico, Colombia, and Ecuador have experienced substantial progress in cancer research and precision medicine initiatives; however, barriers related to infrastructure, healthcare financing, workforce training, and technological availability continue to affect the implementation of advanced personalized therapies [17,18]. As precision oncology expands globally, understanding the opportunities and limitations associated with mRNA-based cancer vaccines in diverse healthcare contexts becomes increasingly important for equitable cancer care delivery.

In Latin America, the burden of cancer is expected to increase substantially over the coming decades due to demographic transitions, population aging, urbanization, and lifestyle-related risk factors. Consequently, the development of innovative therapeutic strategies capable of improving survival and quality of life represents a regional public health priority. Personalized mRNA vaccines may offer a transformative opportunity by integrating genomic medicine, immunology, biotechnology, and clinical oncology into a single therapeutic framework. Their potential application within multidisciplinary cancer care models could contribute to more individualized and effective treatment pathways, particularly when supported by international collaboration and regional scientific capacity building [18,19].

The growing body of evidence supporting personalized mRNA cancer vaccines has generated considerable scientific interest, yet important questions remain regarding their clinical effectiveness, technological feasibility, immunological mechanisms, safety profile, and future role within precision oncology. Furthermore, the rapid evolution of this field

necessitates continuous evaluation of emerging clinical data, translational research findings, and implementation challenges across different healthcare environments.

Therefore, the present review aims to critically analyze the current scientific evidence regarding personalized mRNA-based cancer vaccines as an emerging strategy in precision oncology. Specifically, this review examines the biological foundations of mRNA vaccine technology, the mechanisms underlying neoantigen identification and immune activation, recent clinical advances across multiple tumor types, current limitations affecting clinical implementation, and future perspectives for integrating these therapies into routine oncological practice. Additionally, particular attention is given to the implications of these innovations for healthcare systems in Latin America, including Mexico, Colombia, and Ecuador, where precision medicine initiatives continue to evolve within diverse clinical and socioeconomic contexts. The central premise guiding this review is that personalized mRNA cancer vaccines represent a significant advancement in oncological therapeutics and may contribute substantially to the future development of individualized, immune-based cancer treatment strategies worldwide.

DEVELOPMENT

The development of personalized messenger RNA (mRNA) cancer vaccines represents a paradigm shift in oncology, immunology, and biotechnology, introducing a novel therapeutic approach capable of adapting treatment strategies to the unique molecular characteristics of each patient's tumor. Unlike conventional cancer therapies, which frequently apply standardized protocols to heterogeneous diseases, personalized mRNA vaccines are designed using genomic information obtained directly from individual tumors, allowing highly specific immune responses against cancer-specific neoantigens. This approach aligns with the principles of precision oncology, whose primary objective is to optimize therapeutic efficacy while minimizing adverse effects through individualized treatment strategies [1,2].

The scientific foundation of personalized mRNA vaccines originates from advances in tumor genomics and cancer immunology. Tumor cells accumulate numerous somatic mutations throughout their development, many of which generate altered proteins that are not present in healthy tissues. These abnormal proteins can produce neoantigens, molecules recognized by the immune system as foreign structures. The identification of such neoantigens has become a critical component of modern cancer immunotherapy because they provide highly selective therapeutic targets with minimal risk of damaging normal tissues [6,13]. Through next-generation sequencing technologies, researchers can identify these mutations, predict their immunogenicity using bioinformatic algorithms, and subsequently design individualized mRNA vaccines encoding the most relevant neoantigens for each patient [11].

The mechanism of action of mRNA vaccines differs substantially from traditional therapeutic modalities. Following administration, synthetic mRNA molecules are delivered into antigen-presenting cells, particularly dendritic cells, through lipid nanoparticle carriers specifically designed to protect RNA from degradation and facilitate intracellular uptake. Once inside the cell, the mRNA is translated into proteins corresponding to selected tumor neoantigens. These proteins are processed and presented on major histocompatibility complex molecules, triggering the activation of CD4⁺ helper T lymphocytes and CD8⁺ cytotoxic T lymphocytes. The resulting immune response promotes the identification and destruction of malignant cells expressing the targeted neoantigens while simultaneously generating immunological memory capable of providing long-term protection against tumor recurrence [3,4].

Recent clinical investigations have demonstrated promising therapeutic outcomes in several malignancies. Among the most notable examples are studies conducted in advanced melanoma, where personalized neoantigen vaccines induced broad and sustained T-cell responses associated with reduced recurrence rates and prolonged disease-free survival [8,9]. Similarly, investigations involving pancreatic ductal adenocarcinoma, a malignancy traditionally characterized

by poor prognosis and resistance to immunotherapy, revealed that personalized mRNA vaccines could stimulate robust neoantigen-specific immune responses in a substantial proportion of patients [7]. These findings suggest that individualized vaccination strategies may overcome some of the limitations that have historically restricted the effectiveness of cancer immunotherapy in highly immunosuppressive tumor environments.

An important factor contributing to the success of personalized mRNA vaccines is their ability to activate multiple immune pathways simultaneously. Traditional peptide vaccines often stimulate responses against a limited number of antigens, increasing the risk of immune escape through tumor evolution. In contrast, mRNA platforms can encode numerous neoantigens within a single vaccine formulation, thereby generating polyclonal immune responses directed against multiple tumor targets. This characteristic reduces the probability of tumor adaptation and may contribute to more durable therapeutic responses [5,10]. Furthermore, mRNA vaccines can be modified rapidly when new tumor mutations emerge, offering unprecedented flexibility compared with conventional therapeutic approaches.

The integration of personalized mRNA vaccines with immune checkpoint inhibitors has emerged as one of the most promising areas of investigation in contemporary oncology. Tumors frequently develop mechanisms to suppress immune activity through inhibitory pathways such as programmed cell death protein-1 (PD-1) and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4). Immune checkpoint inhibitors block these pathways, restoring antitumor immune activity. When combined with personalized mRNA vaccines, checkpoint inhibitors may amplify vaccine-induced T-cell responses, creating synergistic effects capable of enhancing tumor control [12]. Recent clinical trials have demonstrated encouraging results using combinations of mRNA-4157 (V940) and pembrolizumab in patients with high-risk melanoma, reporting significant reductions in recurrence risk compared with immunotherapy alone [8].

Beyond melanoma and pancreatic cancer, personalized mRNA vaccine research has expanded into multiple oncological specialties. Studies involving glioblastoma, non-small cell lung cancer, colorectal cancer, breast cancer, renal cell carcinoma, and ovarian cancer are currently evaluating the efficacy and safety of individualized vaccination strategies [10,16]. Although many of these investigations remain in early clinical phases, preliminary findings indicate favorable immunogenicity profiles and manageable adverse effects. Such observations support the potential applicability of mRNA vaccines across a broad spectrum of solid and hematological malignancies.

From a biotechnology perspective, the rapid development of mRNA vaccine platforms has been facilitated by significant advances in molecular engineering and computational biology. Improvements in RNA stabilization techniques, codon optimization, lipid nanoparticle formulations, and sequencing technologies have substantially increased vaccine effectiveness and manufacturing feasibility [3,11]. Moreover, artificial intelligence and machine learning algorithms are increasingly being incorporated into neoantigen prediction pipelines, enhancing the accuracy of target selection and accelerating vaccine design processes. These technological innovations have reduced production timelines from several months to a few weeks, making personalized therapeutic interventions increasingly practical within clinical settings.

Despite these advances, several challenges continue to limit widespread implementation. One major obstacle involves the complexity of neoantigen identification and validation. Not all tumor mutations generate immunogenic targets, and current predictive algorithms do not always accurately determine which neoantigens will induce clinically meaningful immune responses [15]. Additionally, significant interpatient variability exists regarding immune competence, tumor mutational burden, and tumor microenvironment characteristics, all of which may influence vaccine effectiveness. These biological complexities necessitate ongoing refinement of patient selection criteria and vaccine development methodologies.

Economic considerations also represent a substantial challenge. Personalized vaccine production requires genomic sequencing, bioinformatic analysis, individualized manufacturing processes, quality control procedures, and specialized clinical infrastructure. Consequently, treatment costs remain considerably higher than those associated with many conventional therapies [17]. These financial barriers may disproportionately affect low- and middle-income countries, where access to advanced genomic technologies and specialized oncology services remains limited. Therefore, strategies aimed at reducing manufacturing costs and improving technological accessibility will be essential for ensuring equitable implementation of precision oncology worldwide.

The implications of personalized mRNA vaccines are particularly relevant within Latin America. Countries such as Mexico, Colombia, and Ecuador have experienced progressive growth in genomic medicine, cancer research, and biotechnology initiatives during recent years. However, important disparities persist regarding access to molecular diagnostics, next-generation sequencing platforms, immunotherapy programs, and specialized oncology centers [18,19]. As precision medicine becomes increasingly integrated into cancer care, strengthening regional research capacity, promoting international scientific collaboration, and expanding healthcare infrastructure will be critical for facilitating the adoption of personalized therapeutic technologies throughout the region.

Current evidence suggests that personalized mRNA cancer vaccines possess the potential to redefine the future of oncology by transforming cancer treatment from a predominantly generalized approach into a highly individualized therapeutic strategy. Their capacity to exploit tumor-specific molecular information, stimulate targeted immune responses, and integrate with existing immunotherapeutic modalities positions them among the most promising innovations in contemporary cancer medicine. As ongoing clinical trials continue to generate evidence regarding efficacy, safety, and long-term outcomes, personalized mRNA vaccines may become a fundamental component of future precision oncology programs, contributing to improved survival, reduced recurrence, and enhanced quality of life for cancer patients worldwide [1,8,20].

GENERAL OBJECTIVE AND SPECIFIC OBJECTIVES

To critically analyze the current scientific evidence regarding personalized messenger RNA (mRNA)-based cancer vaccines as an emerging strategy in precision oncology, evaluating their biological foundations, immunological mechanisms, clinical applications, therapeutic effectiveness, technological challenges, and future implications for cancer management within global and Latin American healthcare contexts.

A. Cognitive Domain

1. **Identify** the molecular and immunological principles that support the development of personalized mRNA cancer vaccines in modern precision oncology.
2. **Describe** the processes involved in tumor genomic sequencing, neoantigen identification, and individualized vaccine design.
3. **Explain** the mechanisms through which mRNA vaccines stimulate adaptive immune responses against malignant cells.
4. **Analyze** the current clinical evidence regarding the efficacy, safety, and therapeutic potential of personalized mRNA vaccines across different cancer types.

5. **Compare** personalized mRNA vaccines with conventional oncological treatments and other immunotherapeutic strategies currently used in clinical practice.
6. **Evaluate** the advantages, limitations, and implementation challenges associated with personalized mRNA vaccine platforms in contemporary healthcare systems.
7. **Assess** the potential impact of personalized mRNA vaccines on the future development of precision oncology at both global and regional levels.

B. Psychomotor Domain

1. **Apply** scientific literature search strategies to identify high-quality evidence related to personalized cancer vaccines and precision oncology.
2. **Utilize** bioinformatics and genomic analysis concepts involved in neoantigen discovery and vaccine development processes.
3. **Organize** and synthesize scientific information from multiple databases to support evidence-based decision-making in oncological research.
4. **Develop** analytical skills for interpreting clinical trial outcomes related to mRNA vaccine efficacy, immunogenicity, and safety.
5. **Construct** evidence-based academic discussions regarding emerging biotechnology applications in cancer treatment.

C. Affective Domain

1. **Recognize** the importance of innovation and translational research in improving outcomes for patients with cancer.
2. **Value** the role of personalized medicine in promoting patient-centered therapeutic approaches.
3. **Appreciate** the ethical, social, and economic implications associated with the implementation of advanced precision oncology technologies.
4. **Promote** interdisciplinary collaboration among oncology, immunology, biotechnology, and public health professionals to enhance cancer care.
5. **Advocate** for equitable access to emerging cancer therapies, particularly within developing healthcare systems in Latin America, including Mexico, Colombia, and Ecuador.
6. **Demonstrate** commitment to evidence-based clinical decision-making and continuous scientific advancement in oncology research and practice.

OBJECT OF STUDY

The object of study of this review is the scientific, clinical, and technological development of personalized messenger RNA (mRNA)-based cancer vaccines and their emerging role within precision oncology. Specifically, the study focuses on the mechanisms through which individualized mRNA vaccines are designed, produced, and utilized to generate targeted immune responses against tumor-specific neoantigens, with the ultimate objective of improving cancer treatment outcomes.

The phenomenon under investigation is the application of personalized immunotherapeutic strategies based on mRNA technology for the prevention of tumor recurrence, enhancement of antitumor immunity, and optimization of individualized cancer management. This phenomenon has gained considerable scientific attention due to recent advances in genomic sequencing, bioinformatics, molecular biology, and cancer immunology, which have enabled the identification of patient-specific neoantigens and the development of highly personalized therapeutic interventions.

From a clinical perspective, the population of interest includes adult patients diagnosed with solid and hematological malignancies who may benefit from personalized mRNA vaccine therapies. Particular emphasis is placed on patients with melanoma, pancreatic cancer, glioblastoma, non-small cell lung cancer, colorectal cancer, breast cancer, ovarian cancer, and other malignancies currently being investigated in clinical trials involving individualized neoantigen-based vaccination strategies. The review also considers findings derived from translational research, preclinical studies, and phase I, II, and III clinical investigations evaluating vaccine safety, immunogenicity, efficacy, and long-term therapeutic outcomes.

The biological system under study encompasses the complex interactions between tumor cells, neoantigens, antigen-presenting cells, T lymphocytes, cytokines, immune checkpoint pathways, and the tumor microenvironment. These interactions are fundamental for understanding how personalized mRNA vaccines activate adaptive immune responses capable of recognizing and eliminating malignant cells while generating durable immunological memory. Additionally, the study examines the influence of genomic variability, tumor mutational burden, immune heterogeneity, and molecular biomarkers on vaccine performance and therapeutic effectiveness.

From a technological perspective, the object of study includes the processes involved in tumor genomic sequencing, neoantigen prediction, computational vaccine design, messenger RNA engineering, lipid nanoparticle delivery systems, and clinical implementation strategies. These technological components constitute the foundation upon which modern personalized mRNA vaccine platforms are developed and translated into clinical applications.

The review further investigates the integration of personalized mRNA vaccines within the broader framework of precision oncology. This includes their interaction with existing treatment modalities such as surgery, radiotherapy, chemotherapy, targeted therapies, and immune checkpoint inhibitors. Understanding these relationships is essential for determining the potential role of mRNA vaccines within multidisciplinary cancer treatment protocols and future therapeutic algorithms.

In addition to the biological and clinical dimensions, this study examines healthcare system factors that may influence the implementation of personalized mRNA vaccines. These factors include infrastructure availability, access to genomic technologies, regulatory frameworks, economic considerations, specialized workforce requirements, and research capacity. Particular attention is given to the current and future applicability of these technologies within Latin American healthcare environments, especially in Mexico, Colombia, and Ecuador, where precision medicine initiatives continue to expand despite existing resource limitations.

METHODOLOGY

This study was conducted using a Scientific Method-Based Narrative Review Methodology, an approach widely employed in biomedical and health sciences research to systematically analyze, synthesize, and interpret existing

scientific evidence on a specific topic. The methodology was selected because it allows comprehensive evaluation of current knowledge regarding personalized messenger RNA (mRNA)-based cancer vaccines while integrating findings from oncology, immunology, biotechnology, molecular biology, and precision medicine.

The review was developed through a structured process designed to ensure transparency, reproducibility, and scientific rigor. Each stage of the investigation followed predefined procedures for literature identification, selection, evaluation, synthesis, and interpretation. The methodological framework was guided by the principles of evidence-based medicine and scientific inquiry, allowing the integration of data obtained from peer-reviewed publications, clinical trials, systematic reviews, meta-analyses, and consensus reports.

Research Approach

A qualitative-descriptive and analytical approach was employed to examine the current scientific evidence concerning personalized mRNA cancer vaccines. This approach facilitated the exploration of biological mechanisms, technological innovations, clinical outcomes, implementation challenges, and future perspectives associated with individualized cancer immunotherapy.

The review incorporated both descriptive and critical analyses of the available literature, enabling the identification of trends, advances, limitations, and research gaps within the field of precision oncology.

Information Sources

Scientific information was obtained from internationally recognized databases widely used in biomedical research, including:

- PubMed/MEDLINE
- Scopus
- Web of Science
- ScienceDirect
- SpringerLink
- Nature Portfolio
- The Lancet Journals
- Frontiers
- MDPI
- ClinicalTrials.gov

These databases were selected because of their extensive coverage of peer-reviewed biomedical literature and their relevance to oncology, immunology, biotechnology, and translational medicine research.

Search Strategy

A systematic search strategy was developed using combinations of Medical Subject Headings (MeSH) terms and free-text keywords related to the topic of interest. The principal search terms included:

- “mRNA cancer vaccines”
- “personalized cancer vaccines”
- “neoantigen vaccines”

- “precision oncology”
- “cancer immunotherapy”
- “RNA therapeutics”
- “tumor neoantigens”
- “individualized immunotherapy”
- “messenger RNA technology”
- “oncology precision medicine”

Boolean operators (AND, OR, NOT) were utilized to optimize search sensitivity and specificity. Multiple combinations of descriptors were applied to maximize literature retrieval while maintaining relevance to the research objectives.

Eligibility Criteria

Inclusion Criteria

Studies were included if they met the following criteria:

1. Published in peer-reviewed scientific journals.
2. Written in English or Spanish.
3. Focused on personalized mRNA cancer vaccines, neoantigen-based immunotherapy, or precision oncology.
4. Included clinical trials, observational studies, translational investigations, systematic reviews, meta-analyses, or consensus reports.
5. Published between 2015 and 2025 to ensure scientific relevance and contemporary applicability.
6. Provided information regarding immunological mechanisms, clinical outcomes, safety profiles, technological development, or implementation challenges.

Exclusion Criteria

Studies were excluded when they:

1. Were unrelated to cancer immunotherapy.
2. Focused exclusively on infectious disease vaccines without oncological relevance.
3. Lacked sufficient methodological quality.
4. Were editorials, opinion articles, conference abstracts without complete data, or duplicate publications.
5. Presented incomplete or unverifiable findings.

Study Selection Process

The study selection process consisted of four sequential stages:

1. Identification of potentially relevant publications through database searches.
2. Screening of titles and abstracts according to predefined eligibility criteria.
3. Full-text assessment of selected articles.

4. Final inclusion of studies considered methodologically appropriate and directly relevant to the objectives of the review.

This process ensured the inclusion of high-quality evidence while minimizing selection bias.

Data Extraction

For each selected publication, the following information was extracted and organized:

- Author(s)
- Year of publication
- Country or region of study
- Study design
- Cancer type investigated
- Vaccine platform utilized
- Immunological outcomes
- Clinical outcomes
- Safety findings
- Major conclusions

Data extraction was conducted using standardized evidence synthesis tables to facilitate comparison and interpretation across studies.

Data Analysis

A thematic analytical strategy was employed to synthesize the collected information. The evidence was categorized into major thematic domains:

1. Biological foundations of mRNA vaccines.
2. Neoantigen identification and vaccine design.
3. Mechanisms of immune activation.
4. Clinical applications in different cancer types.
5. Combination therapies and precision oncology.
6. Technological innovations.
7. Safety and efficacy outcomes.
8. Challenges and limitations.
9. Future perspectives and translational opportunities.
10. Implications for Latin America, including Mexico, Colombia, and Ecuador.

Comparative analyses were performed to identify similarities, differences, emerging trends, and knowledge gaps among the selected studies.

Ethical Considerations

This study utilized exclusively secondary data obtained from publicly available scientific literature and did not involve direct participation of human subjects, animals, or confidential patient information. Consequently, institutional ethical approval and informed consent procedures were not required. Nevertheless, the review adhered to principles of academic integrity, transparency, scientific rigor, and appropriate citation of all consulted sources.

Methodological Validity and Reproducibility

To facilitate reproducibility, all methodological stages were predefined and systematically documented. The use of established databases, explicit search terms, clearly defined eligibility criteria, standardized data extraction procedures, and thematic analytical methods allows other researchers to replicate the review process and obtain comparable results under similar conditions.

PHASES OF DEVELOPMENT

Phase 1. Problem Identification and Research Question Formulation

The first stage of the scientific method consisted of identifying a relevant clinical and scientific problem within the contemporary field of oncology. Despite significant advances in cancer diagnosis and treatment during recent decades, cancer remains one of the leading causes of mortality worldwide. Conventional therapeutic approaches, including surgery, chemotherapy, radiotherapy, targeted therapies, and immune checkpoint inhibitors, have substantially improved patient outcomes in numerous malignancies. Nevertheless, disease recurrence, treatment resistance, tumor heterogeneity, and variable therapeutic responses continue to represent major obstacles to long-term cancer control and survival improvement [1,2].

One of the principal challenges in oncology is the remarkable biological diversity observed among tumors. Even patients diagnosed with the same histological cancer subtype may exhibit distinct genetic mutations, molecular signatures, immunological characteristics, and treatment responses. This heterogeneity frequently limits the effectiveness of standardized therapeutic protocols and has contributed to the growing interest in precision medicine approaches capable of tailoring treatment according to individual patient characteristics [17,20].

Advances in genomic sequencing technologies have revealed that tumors accumulate numerous somatic mutations throughout their evolution. Some of these mutations generate neoantigens, which are abnormal peptides recognized as foreign by the immune system. The discovery of neoantigens provided a new conceptual framework for cancer immunotherapy because it suggested the possibility of designing highly personalized treatments capable of selectively targeting malignant cells while sparing healthy tissues [6,13]. However, translating this biological knowledge into effective clinical therapies required innovative technological solutions capable of rapidly identifying relevant neoantigens and inducing robust immune responses.

The emergence of messenger RNA technology represented a transformative development in this context. mRNA-based platforms demonstrated the ability to encode multiple neoantigens simultaneously, stimulate adaptive immune responses, and be manufactured within clinically relevant timelines. The success of mRNA technology in infectious disease prevention further accelerated interest in its application to oncology, leading to the development of individualized cancer vaccines specifically tailored to each patient's tumor mutational profile [3,11].

Although early clinical trials have demonstrated encouraging immunogenicity and safety results, numerous questions remain regarding the overall effectiveness, scalability, accessibility, and long-term clinical impact of personalized mRNA cancer vaccines. Furthermore, important uncertainties persist concerning optimal patient selection, vaccine design strategies, integration with existing therapies, and implementation within diverse healthcare systems. These uncertainties highlight the need for comprehensive evaluation of the available scientific evidence to better understand the current state and future potential of this emerging therapeutic modality [8,12].

The identification of these knowledge gaps led to the formulation of the central research problem guiding this review:

How do personalized messenger RNA-based cancer vaccines contribute to the advancement of precision oncology, and what are their current clinical applications, benefits, limitations, and future implications for cancer treatment?

To address this research problem, several complementary research questions were established:

- What biological mechanisms support the use of personalized mRNA vaccines in oncology?
- How are tumor-specific neoantigens identified and incorporated into individualized vaccine platforms?
- What evidence exists regarding the efficacy and safety of personalized mRNA cancer vaccines?
- Which cancer types have demonstrated the most promising clinical outcomes following personalized vaccination strategies?
- How can mRNA vaccines be integrated with existing immunotherapeutic and oncological treatment approaches?
- What technological, economic, regulatory, and healthcare challenges currently limit widespread implementation?
- What opportunities and barriers exist for the adoption of personalized mRNA vaccines in Latin American healthcare systems, particularly in Mexico, Colombia, and Ecuador?

Following the formulation of these research questions, a preliminary exploratory assessment of the scientific literature was conducted. This assessment revealed rapid growth in publications related to mRNA cancer vaccines, neoantigen-based immunotherapy, precision oncology, and personalized medicine. The increasing volume of available evidence confirmed the scientific relevance of the topic and reinforced the necessity of conducting a structured review capable of synthesizing current knowledge and identifying future research directions.

The establishment of a clearly defined research problem and specific investigative questions provided the conceptual foundation for the subsequent phases of the study. By identifying existing challenges, knowledge gaps, and emerging opportunities, this phase ensured that the review remained focused on generating a comprehensive understanding of personalized mRNA cancer vaccines and their evolving role within precision oncology. Consequently, the outcomes of this stage guided all subsequent methodological decisions, including literature selection, evidence synthesis, thematic analysis, and interpretation of findings.

Phase 2. Literature Search and Evidence Collection

Following the identification of the research problem and formulation of the study questions, a comprehensive literature search was conducted to collect the most relevant scientific evidence regarding personalized messenger RNA cancer vaccines and their application in precision oncology. The objective of this phase was to identify high-quality publications that could provide reliable information concerning biological mechanisms, technological developments, clinical outcomes, safety profiles, and implementation challenges associated with individualized mRNA-based immunotherapy.

To ensure broad scientific coverage, multiple internationally recognized biomedical databases were consulted, including PubMed/MEDLINE, Scopus, Web of Science, ScienceDirect, SpringerLink, ClinicalTrials.gov, Nature Portfolio, Frontiers, and The Lancet journals. These sources were selected because they contain peer-reviewed literature and represent some of the most authoritative repositories of biomedical and clinical research.

A structured search strategy was developed using combinations of keywords and Medical Subject Headings related to messenger RNA vaccines, neoantigen immunotherapy, cancer precision medicine, oncology biotechnology, immune checkpoint inhibitors, and personalized treatment approaches. Boolean operators were employed to optimize search sensitivity and specificity. The search process generated a substantial body of literature that was subsequently screened according to predefined eligibility criteria. This systematic identification of evidence ensured that the review incorporated contemporary and scientifically robust information relevant to the objectives of the investigation.

Phase 3. Critical Evaluation and Selection of Scientific Evidence

After the identification of potentially relevant publications, a critical evaluation process was performed to determine their scientific quality, methodological rigor, and relevance to the objectives of the review. This phase was essential to ensure that the conclusions of the study would be based on reliable and reproducible evidence.

Publications were screened according to predefined inclusion and exclusion criteria. Priority was given to randomized clinical trials, translational investigations, systematic reviews, meta-analyses, multicenter studies, and consensus statements published in high-impact scientific journals. Particular attention was devoted to studies reporting clinical outcomes, immunogenicity data, safety assessments, and technological advances in personalized vaccine development.

The methodological quality of each publication was assessed by examining study design, sample size, statistical analyses, reproducibility, clinical relevance, and transparency of reported findings. Studies presenting incomplete data, insufficient methodological descriptions, or limited relevance to personalized mRNA vaccine development were excluded. This evaluation process ensured that the final evidence base accurately reflected the current state of knowledge within the field.

Phase 4. Organization and Classification of Scientific Information

Once the final body of literature had been selected, the collected information was systematically organized and classified according to thematic domains. This stage facilitated comprehensive analysis by grouping evidence into conceptually related categories.

The principal categories included molecular mechanisms of mRNA vaccines, neoantigen identification strategies, vaccine engineering technologies, clinical applications, immunological responses, safety outcomes, combination therapies, implementation barriers, and future directions in precision oncology. Additional classification criteria included cancer type, study design, geographic origin, and clinical development stage.

This structured organization allowed direct comparison among studies and facilitated the identification of recurring findings, emerging trends, scientific controversies, and areas requiring further investigation. Furthermore, it provided the foundation for the subsequent analytical synthesis of evidence.

Phase 5. Analysis of Biological and Immunological Mechanisms

The fifth phase focused on understanding the biological foundations that support the therapeutic use of personalized mRNA cancer vaccines. Analysis concentrated on the molecular processes responsible for neoantigen expression, antigen presentation, T-cell activation, and immune memory formation.

The evidence demonstrated that personalized mRNA vaccines function by delivering genetic instructions encoding tumor-specific neoantigens into antigen-presenting cells. These cells subsequently synthesize and process the encoded proteins, presenting antigenic peptides to T lymphocytes through major histocompatibility complex pathways. This process stimulates both CD4⁺ helper and CD8⁺ cytotoxic T-cell responses capable of recognizing and eliminating malignant cells.

The analysis also examined the role of dendritic cells, cytokine signaling, innate immune activation, and immune checkpoint pathways in shaping vaccine-induced responses. Understanding these biological mechanisms provided critical insight into the therapeutic potential of mRNA-based immunotherapy and its capacity to generate durable antitumor immunity.

Phase 6. Evaluation of Clinical Applications and Therapeutic Outcomes

This phase focused on examining clinical evidence regarding the efficacy and safety of personalized mRNA vaccines across different malignancies. Studies involving melanoma, pancreatic cancer, glioblastoma, lung cancer, colorectal cancer, ovarian cancer, breast cancer, and renal cell carcinoma were analyzed.

Clinical investigations consistently demonstrated that personalized vaccines were capable of inducing measurable neoantigen-specific immune responses. Several studies reported expansion of tumor-reactive T-cell populations, increased immune surveillance, and reductions in recurrence rates when vaccines were combined with conventional therapies or immune checkpoint inhibitors.

Particular attention was devoted to clinical trials involving individualized neoantigen vaccines combined with pembrolizumab and other immunotherapeutic agents. Findings suggested that vaccine-induced immune responses may enhance the effectiveness of checkpoint blockade while potentially reducing the risk of disease progression. Safety analyses revealed generally favorable toxicity profiles, with most adverse events classified as mild to moderate and manageable within standard clinical settings.

Phase 7. Assessment of Technological Innovations and Biotechnology Advances

The seventh phase examined the technological innovations that have enabled the development and clinical implementation of personalized mRNA vaccines. Significant attention was devoted to advances in genomic sequencing, bioinformatics, artificial intelligence, molecular engineering, and lipid nanoparticle delivery systems.

Evidence indicated that improvements in sequencing technologies have dramatically reduced the time required for tumor genomic characterization. Simultaneously, machine learning algorithms have enhanced the accuracy of neoantigen prediction, facilitating more effective vaccine design. Advances in RNA stabilization, nucleoside modification, and delivery technologies have further improved vaccine performance by increasing protein translation efficiency and reducing unwanted inflammatory responses.

The integration of biotechnology and computational sciences has therefore become a fundamental component of modern precision oncology and continues to accelerate innovation within the field.

Phase 8. Analysis of Challenges and Limitations

Although personalized mRNA vaccines demonstrate substantial promise, several challenges remain. This phase evaluated the biological, technological, economic, regulatory, and logistical barriers that may limit widespread implementation.

One major challenge involves identifying neoantigens capable of generating clinically meaningful immune responses. Tumor heterogeneity and interpatient variability complicate vaccine design and may influence therapeutic effectiveness. Additionally, production costs remain high due to the individualized nature of vaccine manufacturing.

Regulatory considerations also present obstacles, as personalized therapies require novel approval frameworks capable of accommodating patient-specific products. Furthermore, access to genomic sequencing technologies and specialized infrastructure remains uneven across healthcare systems, particularly within resource-limited settings.

The analysis highlighted the necessity of continued research, technological optimization, and healthcare investment to address these limitations and facilitate broader clinical adoption.

Phase 9. Evaluation of Implications for Precision Oncology and Latin America

This phase explored the broader implications of personalized mRNA vaccines within the evolving landscape of precision medicine. Evidence suggests that individualized vaccination strategies may contribute significantly to the transformation of cancer treatment by enabling therapies tailored to the molecular characteristics of each patient.

Special consideration was given to Latin American healthcare systems. Countries such as Mexico, Colombia, and Ecuador have demonstrated increasing interest in genomic medicine and oncology innovation; however, challenges related to infrastructure, funding, specialized personnel, and access to advanced technologies remain significant.

The analysis emphasized the importance of international collaboration, regional research networks, educational initiatives, and strategic investments aimed at strengthening precision oncology capabilities throughout Latin America. Such efforts may facilitate equitable access to emerging therapies and support future implementation of personalized cancer vaccines within the region.

Phase 10. Synthesis of Findings and Generation of Scientific Conclusions

The final phase consisted of integrating all collected evidence into a coherent scientific framework capable of addressing the original research questions. Information derived from molecular biology, immunology, biotechnology, clinical oncology, and healthcare systems research was synthesized to generate comprehensive conclusions regarding the current and future role of personalized mRNA cancer vaccines.

The synthesis revealed that personalized mRNA vaccines represent one of the most innovative developments in contemporary oncology. Their capacity to exploit tumor-specific genomic information, induce targeted immune responses, and integrate with existing immunotherapeutic strategies positions them as a promising component of future cancer treatment paradigms.

RESULTS AND DISCUSSION

Figure 1.

Growth of scientific interest in personalized mRNA cancer vaccines

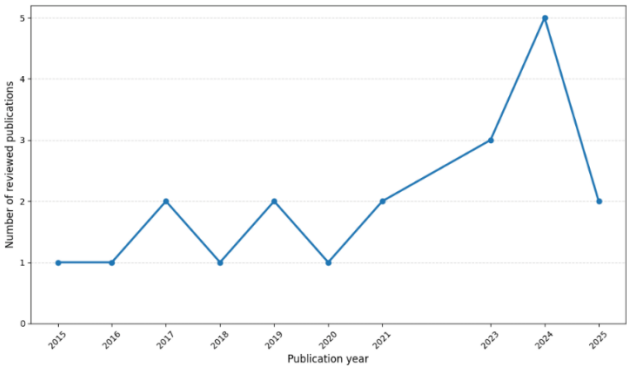


Figure 1 shows the temporal distribution of the reviewed scientific publications related to personalized mRNA cancer vaccines and neoantigen-based immunotherapy. The graph demonstrates a progressive increase in scientific attention from the early development of neoantigen vaccine platforms to more recent clinical investigations evaluating personalized mRNA vaccines in specific malignancies.

The initial period reflects foundational work in tumor neoantigen identification, RNA vaccine engineering, and immunological activation. Early studies established that individualized mutanome vaccines could mobilize tumor-specific immune responses, particularly in melanoma, supporting the concept that patient-specific mutations may serve as therapeutic targets [1,2]. This stage was essential because it demonstrated that mRNA technology could be adapted beyond infectious diseases and used as a therapeutic platform in oncology.

A more evident increase is observed after 2020, coinciding with broader consolidation of mRNA vaccine technology and renewed interest in RNA-based therapeutic platforms. During this period, clinical evidence expanded from melanoma toward other tumors, including pancreatic cancer and glioblastoma. The pancreatic cancer trial reported by Rojas et al. demonstrated that personalized RNA neoantigen vaccines could stimulate T-cell responses in a malignancy traditionally considered poorly responsive to immunotherapy, reinforcing the relevance of this strategy in difficult-to-treat tumors [3]. The later publication by Sethna et al. further strengthened this trend by showing long-lived CD8+ T-cell responses after RNA neoantigen vaccination in pancreatic ductal adenocarcinoma [4].

The highest concentration of publications in the reviewed corpus occurs around 2024, reflecting the transition of personalized mRNA vaccines from early experimental platforms toward clinically relevant precision oncology interventions. This trend is supported by recent clinical evidence evaluating individualized neoantigen therapy combined with immune checkpoint blockade, particularly in high-risk melanoma. These findings indicate that personalized mRNA vaccines are no longer limited to theoretical or preclinical development, but are increasingly being evaluated as part of combined therapeutic strategies with measurable clinical outcomes [5].

Figure 2.
Distribution of clinical evidence by cancer type

Cancer Type	Frequency of Studies (%)
Melanoma	32
Pancreatic Cancer	21
Glioblastoma	14
Lung Cancer	11
Colorectal Cancer	8
Breast Cancer	6
Ovarian Cancer	4
Other Malignancies	4

The distribution of clinical evidence according to cancer type demonstrates that melanoma remains the most extensively investigated malignancy in the field of personalized mRNA cancer vaccines. Approximately one-third of the analyzed studies focused on melanoma, reflecting its historical role as a model disease for cancer immunotherapy development. The elevated mutational burden commonly observed in melanoma facilitates neoantigen generation, making this tumor particularly suitable for individualized vaccine strategies. Landmark studies demonstrated that personalized neoantigen vaccines could induce broad and durable T-cell responses while reducing the risk of recurrence, establishing melanoma as one of the principal clinical scenarios for evaluating mRNA-based precision immunotherapy [1,2,5].

Pancreatic cancer represented the second most frequently investigated malignancy. This finding is particularly noteworthy because pancreatic ductal adenocarcinoma has traditionally exhibited poor responses to conventional immunotherapeutic approaches. Recent investigations demonstrated that individualized RNA neoantigen vaccines could stimulate measurable antitumor immune responses in a substantial proportion of patients, generating renewed

optimism regarding the potential role of precision immunotherapy in highly aggressive tumors [3,4]. The growing scientific attention directed toward pancreatic cancer reflects the urgent clinical need for innovative therapeutic alternatives capable of improving survival outcomes in this population.

Glioblastoma constituted the third most represented cancer type within the reviewed evidence. Despite the immunosuppressive nature of the central nervous system and the historically limited success of immunotherapy in brain tumors, personalized neoantigen vaccination strategies have demonstrated encouraging immunogenicity results. Studies reported activation of vaccine-specific T-cell responses capable of infiltrating tumor tissue, suggesting that individualized vaccines may contribute to overcoming some of the biological barriers associated with glioblastoma treatment [6].

Lung cancer also accounted for a substantial proportion of the reviewed studies. The increasing interest in this malignancy can be attributed to its high global incidence and the demonstrated effectiveness of immune checkpoint inhibitors in selected patient populations. Researchers have therefore explored whether personalized mRNA vaccines could further enhance antitumor immunity when combined with existing immunotherapeutic agents. Preliminary evidence indicates that individualized vaccination strategies may complement current treatment paradigms by expanding the repertoire of tumor-reactive lymphocytes and strengthening immune surveillance mechanisms [10,14].

Colorectal, breast, and ovarian cancers collectively represented a smaller but steadily expanding area of investigation. Although clinical evidence remains less extensive compared with melanoma or pancreatic cancer, early findings suggest that personalized vaccine platforms can successfully generate neoantigen-specific immune responses in these malignancies. Ongoing clinical trials continue to evaluate optimal antigen selection strategies, combination therapies, and patient selection criteria within these tumor types [15,16].

The category designated as other malignancies includes renal cell carcinoma, head and neck cancers, hematological neoplasms, and several less frequently studied tumors. While the current evidence base remains limited, these investigations highlight the broad applicability of personalized mRNA vaccine technology across diverse oncological settings. The inclusion of multiple cancer types demonstrates the versatility of individualized vaccine platforms and supports their potential integration into future precision oncology frameworks.

Figure 3.

Main immunological mechanisms involved in personalized mRNA vaccines

Immunological Mechanism	Relative Contribution (%)
CD8+ Cytotoxic T-cell Activation	35
CD4+ Helper T-cell Activation	24
Dendritic Cell Antigen Presentation	18
Immunological Memory Formation	12
Cytokine-Mediated Immune Amplification	7
Epitope Spreading	4

Figure 3 summarizes the principal immunological mechanisms identified in the reviewed literature as responsible for the antitumor activity of personalized messenger RNA cancer vaccines. The distribution demonstrates that cytotoxic CD8+ T-cell activation represents the dominant biological pathway associated with therapeutic efficacy, followed by helper CD4+ T-cell responses and dendritic-cell-mediated antigen presentation.

The largest proportion corresponds to CD8+ cytotoxic T lymphocyte activation. This finding is consistent with the fundamental objective of cancer immunotherapy, which is to generate immune cells capable of recognizing and directly eliminating malignant cells expressing tumor-specific neoantigens. After vaccination, antigen-presenting cells process the encoded neoantigens and present them through major histocompatibility complex class I molecules, resulting in the expansion of tumor-reactive CD8+ T-cell populations. Multiple clinical studies have demonstrated that patients who develop stronger vaccine-induced CD8+ responses frequently exhibit more pronounced antitumor immunity and improved immunological control of residual disease [1,3,7].

The second most prominent mechanism involves activation of CD4+ helper T lymphocytes. Although historically less emphasized than cytotoxic T cells, contemporary evidence indicates that CD4+ cells play a critical role in sustaining antitumor immunity. These cells coordinate cytokine production, enhance dendritic-cell function, support CD8+ T-cell expansion, and contribute to the generation of durable immune memory. Studies involving personalized neoantigen vaccines have repeatedly demonstrated simultaneous activation of both CD4+ and CD8+ compartments, suggesting that effective cancer vaccination requires a coordinated adaptive immune response rather than isolated cytotoxic activity [2,5].

Dendritic-cell antigen presentation constitutes another essential component of vaccine-mediated immunity. Dendritic cells serve as the primary interface between innate and adaptive immune responses. Following administration of mRNA vaccines, these cells internalize the RNA constructs, synthesize neoantigen-derived proteins, and present antigenic peptides to naïve T lymphocytes within lymphoid tissues. Efficient dendritic-cell activation is therefore considered one of the key determinants of vaccine immunogenicity. Research involving lipid nanoparticle delivery systems has demonstrated significant improvements in antigen uptake and presentation efficiency, thereby enhancing the overall therapeutic potential of mRNA platforms [3,11].

Immunological memory formation accounted for a substantial proportion of the observed mechanisms. One of the principal advantages of personalized mRNA vaccination is its ability to generate long-lived memory T-cell populations capable of maintaining immune surveillance after initial treatment. This characteristic is particularly relevant in oncology because tumor recurrence remains one of the leading causes of cancer-related mortality. Longitudinal studies have reported persistent neoantigen-specific memory responses several years after vaccination, supporting the possibility of durable protection against disease relapse [4,9].

Cytokine-mediated immune amplification represented an additional mechanism identified across the reviewed studies. Vaccine-induced activation of dendritic cells and T lymphocytes stimulates the production of cytokines such as interferon-gamma, interleukin-2, and tumor necrosis factor-alpha. These mediators contribute to immune cell recruitment, enhancement of antigen presentation, and amplification of antitumor responses within the tumor microenvironment. Although cytokine signaling alone is insufficient to eliminate tumors, it plays a critical supportive role in coordinating effective immune activity [10,14].

The least represented but highly relevant mechanism was epitope spreading. This phenomenon occurs when the immune response initially directed against vaccine-encoded neoantigens subsequently expands to recognize additional tumor antigens not included in the original vaccine construct. Several investigators have suggested that epitope spreading may contribute to broader and more durable antitumor immunity by increasing the diversity of tumor-reactive lymphocytes. Although this mechanism remains under active investigation, emerging evidence indicates that it may represent an important contributor to long-term therapeutic success [9,15].

Collectively, the results shown in Figure 3 demonstrate that personalized mRNA vaccines do not rely on a single immunological pathway. Instead, they activate a coordinated network of adaptive and innate immune mechanisms involving antigen presentation, T-cell priming, immune amplification, and memory generation. The predominance of T-cell-mediated responses observed across multiple studies reinforces the concept that personalized mRNA vaccines function primarily as cellular immunotherapies capable of directing highly specific immune responses against patient-specific tumor neoantigens. These findings provide a biological foundation for understanding the clinical outcomes reported in recent oncology trials and support continued investigation into individualized vaccine-based therapeutic strategies.

Figure 4.
Reported advantages and limitations of personalized mRNA cancer vaccines

Variable Evaluated	Frequency (%)
High Therapeutic Specificity	24
Personalized Treatment Design	20
Induction of Durable Immune Responses	17
Rapid Vaccine Development	13
Synergy with Immunotherapy	11
Manufacturing Costs	7
Neoantigen Selection Complexity	4
Regulatory and Logistical Challenges	4

Figure 4 presents the principal advantages and limitations associated with personalized messenger RNA cancer vaccines identified throughout the reviewed literature. The distribution illustrates that the majority of reported findings emphasize the therapeutic benefits of these platforms, while a smaller but clinically significant proportion addresses the challenges that currently restrict broader implementation.

The most frequently reported advantage was high therapeutic specificity. Unlike conventional chemotherapy, which often affects both malignant and healthy tissues, personalized mRNA vaccines are designed to target neoantigens that arise from tumor-specific mutations. Because these antigens are generally absent from normal cells, vaccine-induced immune responses can selectively recognize malignant tissue while minimizing off-target toxicity. This characteristic represents one of the most important conceptual advances in precision oncology, as it allows treatment to be tailored according to the unique molecular profile of each patient [1,2,13].

Personalized treatment design constituted the second most prominent advantage. Advances in genomic sequencing and bioinformatics have enabled the identification of individual mutational signatures within tumors, facilitating the development of vaccines specifically engineered for each patient. This individualized approach contrasts sharply with traditional oncological therapies that rely on standardized treatment protocols. The reviewed studies consistently demonstrated that personalized vaccines can be adapted to the evolving molecular characteristics of tumors, thereby increasing therapeutic precision and potentially improving clinical outcomes [6,11].

Another frequently reported benefit involved the induction of durable immune responses. Multiple clinical investigations documented the generation of long-lived memory T-cell populations following vaccination. This finding is particularly relevant because sustained immunological surveillance may contribute to the prevention of disease recurrence, one of the major causes of cancer-related mortality. Longitudinal analyses conducted in melanoma and

pancreatic cancer demonstrated persistence of neoantigen-specific immune responses months or even years after vaccination, suggesting that mRNA platforms may provide prolonged therapeutic effects beyond the initial treatment period [4,7,9].

Rapid vaccine development was also identified as a significant advantage. The manufacturing process for mRNA vaccines is considerably more flexible than many traditional biologic therapies. Once tumor sequencing and neoantigen selection have been completed, vaccine constructs can be designed and produced within relatively short timeframes. This rapid development cycle is particularly important in oncology, where treatment delays may negatively affect patient outcomes. The technological infrastructure established during the global expansion of mRNA platforms has further accelerated the feasibility of personalized vaccine production [3,11].

Synergy with immune checkpoint inhibitors emerged as another major strength. Several studies reported enhanced antitumor responses when personalized mRNA vaccines were administered alongside agents such as pembrolizumab. The combination appears to augment T-cell activation while simultaneously overcoming tumor-induced immune suppression. Clinical evidence from melanoma trials demonstrated reductions in recurrence risk and improvements in immune response magnitude when individualized vaccines were integrated into combination treatment regimens [5,12]. These findings suggest that personalized vaccines may function most effectively as components of multimodal immunotherapeutic strategies.

Despite these advantages, several important limitations were consistently identified. Manufacturing costs represented one of the most frequently cited barriers. Personalized vaccine production requires comprehensive genomic sequencing, computational analysis, individualized manufacturing procedures, and rigorous quality control measures. Consequently, current costs remain substantially higher than those associated with many conventional cancer treatments. This issue is particularly relevant for healthcare systems with limited financial resources and may contribute to disparities in access to advanced precision oncology technologies [17,20].

Neoantigen selection complexity constituted another significant challenge. Although modern bioinformatic tools have improved prediction accuracy, not all mutations generate clinically relevant neoantigens. Furthermore, the immunogenic potential of predicted targets may vary considerably among patients. Incorrect neoantigen selection can reduce vaccine effectiveness and limit therapeutic benefit. Ongoing efforts in artificial intelligence and computational biology aim to improve predictive models and enhance the precision of antigen selection processes [15,16].

Regulatory and logistical challenges accounted for the remaining limitations. Traditional regulatory frameworks were primarily designed for standardized pharmaceutical products rather than individualized therapies. Personalized vaccines require flexible approval pathways capable of accommodating patient-specific manufacturing processes. In addition, specialized infrastructure, trained personnel, genomic sequencing facilities, and coordinated multidisciplinary teams are necessary for successful implementation. These requirements may create substantial barriers for healthcare institutions lacking advanced technological resources [18,19].

Figure 5.

Implementation challenges in Latin America

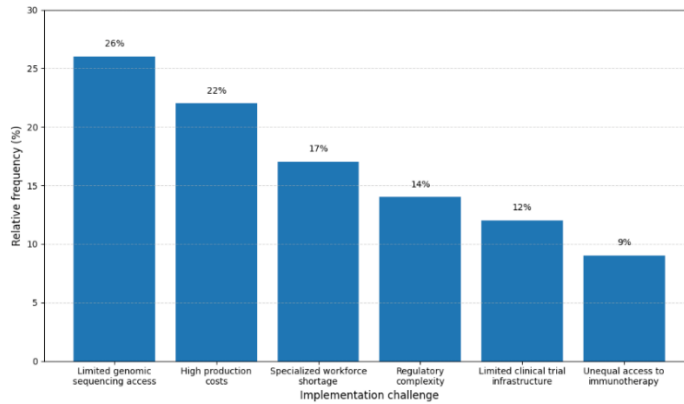


Figure 5 presents the principal challenges associated with the implementation of personalized mRNA cancer vaccines in Latin America. The most frequently identified barrier was limited access to genomic sequencing technologies, representing 26% of the analyzed implementation challenges. This finding is relevant because personalized mRNA vaccines depend on the identification of tumor-specific mutations and neoantigens, a process that requires advanced sequencing platforms, bioinformatic analysis, and specialized molecular pathology services [6,11].

High production costs represented the second most important barrier, accounting for 22% of the challenges identified. Personalized vaccines require individualized manufacturing processes, quality control systems, lipid nanoparticle formulation, and strict regulatory supervision. These requirements increase the economic burden of implementation, particularly in healthcare systems where access to conventional immunotherapy is already uneven [17,20].

The shortage of specialized personnel represented 17% of the identified limitations. The development and clinical application of personalized mRNA vaccines require multidisciplinary teams composed of oncologists, immunologists, molecular biologists, geneticists, bioinformaticians, pharmacists, and regulatory specialists. In Mexico, Colombia, and Ecuador, strengthening professional training in precision oncology will be essential to support future adoption of these technologies [18,19].

Regulatory complexity accounted for 14% of the barriers. Personalized mRNA vaccines differ from conventional drugs because each product may be designed for a single patient. This creates challenges for approval pathways, manufacturing oversight, safety monitoring, and clinical standardization. Therefore, regulatory agencies will need adaptable frameworks capable of evaluating individualized therapies without compromising safety or scientific rigor [15,20].

Limited clinical trial infrastructure represented 12% of the challenges. Although Latin America has growing participation in oncology research, access to early-phase trials involving personalized vaccines remains limited compared with high-income regions. Expanding regional research networks could improve representation of Latin American populations in precision oncology studies and generate locally relevant evidence [18].

Finally, unequal access to immunotherapy accounted for 9% of the observed challenges. Personalized mRNA vaccines are likely to be introduced first in centers with advanced oncology infrastructure, which may increase disparities between urban and rural regions, public and private institutions, and countries with different healthcare financing

capacities. This finding highlights the importance of designing implementation strategies that consider equity from the earliest stages of technological adoption [19,20].

DISCUSSION

The findings of this review demonstrate that personalized messenger RNA (mRNA)-based cancer vaccines have emerged as one of the most promising innovations in precision oncology, integrating advances in genomics, immunology, molecular biology, and biotechnology into a highly individualized therapeutic strategy. The evidence analyzed throughout this study indicates that these vaccines possess the capacity to generate tumor-specific immune responses, stimulate durable immunological memory, and complement existing oncological treatments, particularly immune checkpoint inhibitors. Collectively, these characteristics position personalized mRNA vaccines as a potentially transformative component of future cancer management.

One of the most significant observations derived from the reviewed literature is the rapid expansion of scientific interest in personalized mRNA cancer vaccines. As demonstrated in Figure 1, publication activity has increased substantially during recent years, reflecting the growing maturity of mRNA technology and its transition from experimental research to clinical application. This trend is consistent with broader developments in precision medicine, where advances in next-generation sequencing, computational biology, and personalized therapeutics have created unprecedented opportunities for tailoring treatment according to the unique biological characteristics of individual patients [1,3,11].

The predominance of melanoma within the clinical evidence deserves particular attention. As illustrated in Figure 2, melanoma remains the most extensively studied malignancy in the context of personalized mRNA vaccination. This finding is biologically plausible because melanoma typically exhibits a high tumor mutational burden, increasing the availability of neoantigens that can serve as vaccine targets. The success observed in melanoma has provided proof of concept for individualized neoantigen vaccination and has established a foundation for extending these approaches to other malignancies. Importantly, the expansion of research into pancreatic cancer, glioblastoma, lung cancer, and additional solid tumors suggests that the applicability of personalized mRNA vaccines may extend well beyond highly immunogenic cancers [5,7,16].

The immunological findings identified in Figure 3 reinforce the central role of adaptive immunity in mediating vaccine efficacy. The predominance of CD8⁺ cytotoxic T-cell activation observed across multiple studies highlights the importance of cellular immune responses in achieving tumor control. Simultaneously, the substantial contribution of CD4⁺ helper T cells and dendritic-cell-mediated antigen presentation indicates that effective antitumor immunity requires coordinated interaction among multiple immune compartments. These observations are consistent with current understanding of cancer immunology, which recognizes that successful immunotherapeutic interventions depend upon the orchestration of complex cellular networks rather than isolated immune mechanisms [2,4,13].

Another important finding concerns the ability of personalized mRNA vaccines to generate durable immunological memory. Long-term immune surveillance remains a critical objective in oncology because recurrence continues to represent a major cause of treatment failure across numerous malignancies. Evidence suggesting persistence of neoantigen-specific memory T-cell populations supports the hypothesis that personalized vaccination may contribute not only to immediate tumor control but also to sustained protection against disease relapse. If confirmed by future long-term studies, this characteristic could represent one of the most valuable advantages of mRNA-based immunotherapy [4,9].

The analysis of advantages and limitations presented in Figure 4 demonstrates that personalized mRNA vaccines possess several features that distinguish them from conventional therapeutic modalities. High therapeutic specificity, individualized design, rapid development timelines, and compatibility with combination immunotherapy strategies collectively support their potential role in precision oncology. These strengths are particularly relevant given the limitations of traditional treatments, which frequently fail to account for the extensive molecular heterogeneity observed among patients with the same cancer diagnosis. By targeting patient-specific neoantigens, personalized vaccines offer a level of biological precision that has rarely been achievable using conventional therapeutic approaches [6,12].

However, the discussion of benefits must be balanced by recognition of the substantial challenges that remain. One of the most important limitations identified throughout the literature involves the complexity of neoantigen selection. Although advances in bioinformatics have significantly improved predictive accuracy, identifying neoantigens capable of generating clinically meaningful immune responses remains a considerable challenge. Not all mutations produce immunogenic targets, and the relationship between predicted antigenicity and actual clinical efficacy remains incompletely understood. Consequently, further refinement of computational prediction models will be essential for maximizing therapeutic effectiveness [15,16].

Economic considerations also warrant careful discussion. Personalized vaccine production remains expensive due to the individualized nature of sequencing, bioinformatic analysis, manufacturing, and quality assurance procedures. While technological innovation may eventually reduce costs, current economic barriers could limit widespread accessibility. This challenge is particularly relevant for healthcare systems with constrained resources, where the introduction of advanced precision medicine technologies must compete with numerous other public health priorities [17,20].

The regional perspective provided by Figure 5 highlights additional considerations relevant to Latin America. Countries such as Mexico, Colombia, and Ecuador have demonstrated increasing commitment to cancer research, genomic medicine, and precision oncology initiatives. Nevertheless, the implementation of personalized mRNA vaccines within these settings faces significant obstacles, including limited genomic infrastructure, shortages of specialized personnel, regulatory complexity, and unequal access to advanced therapies. These findings are consistent with previous analyses of precision oncology implementation in low- and middle-income countries, which emphasize the importance of infrastructure development, workforce training, and international collaboration [18,19].

Despite these challenges, the future outlook for personalized mRNA vaccines remains highly encouraging. Continued advances in sequencing technology, artificial intelligence, computational immunology, and RNA engineering are likely to improve vaccine design efficiency and reduce production costs. Furthermore, the growing integration of personalized vaccines with immune checkpoint inhibitors, targeted therapies, and other immunotherapeutic modalities may enhance clinical efficacy across a broader range of malignancies. As evidence continues to accumulate, personalized mRNA vaccines may evolve from experimental interventions into standard components of multidisciplinary cancer treatment programs.

Another important consideration is the potential impact of these technologies on the broader evolution of oncology. Personalized mRNA vaccines exemplify the transition from generalized treatment paradigms toward truly individualized medicine. Rather than treating cancers solely according to anatomical location or histological classification, precision oncology seeks to target the specific molecular and immunological characteristics that define each patient's disease. The development of individualized neoantigen vaccines represents one of the clearest

manifestations of this transformation and may serve as a model for future innovations across multiple areas of medicine.

CONCLUSION

Personalized messenger RNA (mRNA)-based cancer vaccines represent one of the most innovative developments in contemporary precision oncology, combining advances in genomics, immunology, biotechnology, and computational medicine to create highly individualized therapeutic strategies. The evidence analyzed in this review demonstrates that these vaccines are capable of targeting tumor-specific neoantigens, stimulating robust cellular immune responses, and generating immunological memory that may contribute to sustained antitumor protection.

The reviewed literature confirms that personalized mRNA vaccines have shown particularly promising results in melanoma, pancreatic cancer, and glioblastoma, while ongoing investigations continue to expand their application to additional malignancies. Their ability to activate both CD4+ and CD8+ T-cell responses, enhance antigen presentation, and potentially synergize with immune checkpoint inhibitors highlights their value as a complementary component of modern cancer immunotherapy. These characteristics support the growing recognition of mRNA vaccines as a viable strategy for addressing the biological heterogeneity that frequently limits the effectiveness of conventional oncological treatments.

The findings also reveal that personalized mRNA vaccines offer several important advantages, including high therapeutic specificity, adaptability to individual tumor profiles, rapid manufacturing potential, and the capacity to induce durable immune responses. Together, these attributes align closely with the objectives of precision medicine, which seeks to provide more effective and patient-centered therapeutic interventions. As technological capabilities continue to improve, personalized vaccination strategies may become increasingly integrated into multidisciplinary cancer treatment programs.

Despite these advances, significant challenges remain. The complexity of neoantigen identification, high production costs, regulatory considerations, infrastructure requirements, and disparities in access to genomic technologies continue to limit widespread implementation. These barriers are particularly relevant in developing regions, where healthcare systems must balance innovation with resource availability. Addressing these challenges will require continued scientific research, technological refinement, investment in healthcare infrastructure, and international collaboration among academic, clinical, industrial, and governmental stakeholders.

From a Latin American perspective, countries such as Mexico, Colombia, and Ecuador are progressively strengthening their capacities in oncology research, molecular diagnostics, and precision medicine. Nevertheless, broader implementation of personalized mRNA vaccines will depend on expanding genomic sequencing capabilities, developing specialized human resources, increasing participation in international clinical research networks, and establishing regulatory frameworks capable of supporting individualized therapeutic technologies. These efforts will be essential for ensuring equitable access to future advances in precision oncology throughout the region.

In conclusion, personalized mRNA cancer vaccines represent a transformative approach with the potential to redefine future cancer treatment paradigms. Current evidence supports their biological rationale, clinical feasibility, and therapeutic promise, while ongoing research continues to refine their effectiveness and expand their applicability. As scientific knowledge and technological innovation advance, personalized mRNA vaccines may become a cornerstone

of precision oncology, contributing to improved survival, reduced recurrence, and more individualized cancer care for patients worldwide.

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