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Personalized Surgery in Oncology: Integration of Genomic Biomarkers and Vaccinal Therapies as Surgical Adjuvants

Cirugía personalizada en oncología: integración de biomarcadores genómicos y terapias vacunales como adyuvantes quirúrgicos

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Resumen

La resección quirúrgica es la opción curativa principal para muchos tumores sólidos, pero la recurrencia sigue siendo alta por la enfermedad micrometastásica que la cirugía convencional no elimina por completo. La oncología de precisión permite integrar biomarcadores genómicos y estrategias inmunológicas personalizadas para optimizar resultados quirúrgicos. Este estudio evaluó combinar perfil genómico y vacunas personalizadas basadas en neoantígenos como coadyuvantes perioperatorios para reducir recurrencia y prolongar la supervivencia libre de enfermedad. Se empleó un enfoque documental, estadístico y experimental para identificar mutaciones frecuentes y valorar su potencial inmunogénico. Un heatmap de afinidad predijo la interacción entre neoantígenos y alelos MHC, y un ensayo in vitro confirmó lisis celular tras la exposición al prototipo vacunal. Las proyecciones estadísticas y una curva simulada de Kaplan–Meier mostraron que sumar una vacuna personalizada a la cirugía guiada por biomarcadores podría reducir la recurrencia hasta un 50 % y aumentar la supervivencia libre de enfermedad de 24 a 40 meses. Estos resultados coinciden con evidencia previa que respalda las vacunas de neoantígenos como herramienta para potenciar la respuesta inmune contra células tumorales residuales, complementando la resección precisa. Aunque los hallazgos son prometedores, se requieren estudios in vivo y ensayos clínicos para confirmar seguridad, eficacia y viabilidad, especialmente en contextos con infraestructura limitada. Este trabajo respalda que integrar perfil molecular, diseño vacunal y planificación quirúrgica personalizada puede fortalecer la oncología de precisión y mejorar mayores posibilidades de remisión prolongada.

Palabras clave: Oncología de Precisión, Biomarcadores Genómicos, Vacuna de Neoantígenos, Cirugía Oncológica, Riesgo de Recurrencia.

Abstract

Surgical resection remains the main curative option for many solid tumors, but recurrence is still high due to micrometastatic disease that conventional surgery alone cannot fully remove. Precision oncology now makes it possible to integrate genomic biomarkers and personalized immunological strategies to improve surgical results. This study evaluated combining genomic profiling and personalized neoantigen-based vaccines as perioperative adjuvants to lower recurrence and extend disease-free survival. A documentary, statistical, and experimental approach identified frequent mutations and assessed their immunogenic potential. A binding affinity heatmap predicted interactions between neoantigens and MHC alleles, and an in vitro assay confirmed tumor cell lysis after exposure to the prototype vaccine. Statistical projections and a simulated Kaplan–Meier curve showed that adding a personalized vaccine to biomarker-guided surgery could reduce recurrence by up to 50% and increase disease-free survival from 24 to 40 months. These findings align with existing evidence that neoantigen vaccines help boost the immune response against residual tumor cells, complementing precise surgical removal. Although the results are promising, in vivo studies and clinical trials are needed to confirm safety, real effectiveness, and feasibility, especially in settings with limited genomic resources. This work supports that combining molecular profiling, rational vaccine design, and tailored surgical planning can strengthen precision oncology and offer patients a better chance of achieving long-lasting remission.

Keywords: Precision Oncology, Genomic Biomarkers, Neoantigen Vaccine, Cancer Surgery, Recurrence Risk.

1. Introducción

Personalized surgery in oncology represents a paradigm shift toward tailoring cancer treatment to each patient's unique molecular and immunological profile. Traditional oncologic surgery has been fundamentally effective for local tumor control, but persistent challenges such as recurrence, metastasis, and treatment resistance highlight its limitations when applied as an isolated strategy (Sledge et al., 2020; Vogelstein et al., 2013). As the cancer burden continues to grow globally, there is an urgent need to expand the therapeutic potential of surgical interventions through precise, evidence-based integration of complementary modalities (Miller et al., 2022).

A key driver of this transformation is the advent of genomic biomarkers, which have enabled unprecedented characterization of tumor heterogeneity and clonal evolution (Vogelstein et al., 2013; Van Allen et al., 2014). Whole-exome sequencing and other molecular profiling technologies have demonstrated that actionable mutations can directly inform surgical planning, perioperative risk assessment, and adjuvant treatment selection (Krag et al., 2020; Van Allen et al., 2014). For instance, mutations affecting DNA repair pathways, such as mismatch repair deficiency, have been linked to higher immunogenicity and better responses to immunotherapies (Le et al., 2017; Topalian et al., 2012). This insight underscores the potential of integrating biomarker data with immunological strategies in the surgical setting.

In parallel, the rapid evolution of immunotherapy has transformed the management of advanced malignancies, establishing immune checkpoint inhibitors and adoptive cell transfer as pivotal tools for durable tumor control (Topalian et al., 2012; Rosenberg et al., 2008; Brahmer et al., 2018). However, the perioperative window remains an underexploited opportunity for harnessing the immune system to eradicate micrometastatic disease and residual tumor cells that often cause recurrence (Ott et al., 2017; Eggermont et al., 2018). Recent studies show that perioperative immunosuppression, wound healing dynamics, and tumor microenvironment changes after surgery may influence relapse risk, making this window ideal for immune modulation (Chen & Mellman, 2017; Mellman et al., 2011).

Within this context, cancer vaccines have re-emerged as promising agents for generating tumor-specific immune responses with high precision (Butterfield, 2015; Melief et al., 2015). Unlike traditional vaccines, therapeutic cancer vaccines target tumor neoantigens—mutations unique to each patient's tumor—offering unprecedented specificity (Sahin et al., 2017; Schumacher et al., 2015). Early-phase clinical trials combining neoantigen vaccines with immune checkpoint blockade have shown encouraging results, demonstrating synergistic anti-tumor effects (Rech et al., 2016; Hu et al., 2018). Pioneering work has established that RNA mutanome vaccines can mobilize poly-specific cytotoxic T cells capable of recognizing and destroying residual cancer cells post-resection (Sahin et al., 2017; Schumacher et al., 2015).

Parallel to technological advances, the expanding body of evidence on pathways such as mTOR signaling and nutrient sensing further illustrates how cellular metabolism intersects with tumor progression and immunoresponsiveness (Sabatini, 2017). These insights inform the development of biomarkers capable of predicting which patients may derive maximum benefit from combined surgical-immunological approaches (Krag et al., 2020; Van Allen et al., 2014).

While early vaccination trials focused on virus-induced cancers such as HPV-related lesions have validated the therapeutic potential of antigen-specific vaccination (Kenter et al., 2009; Mellman et al., 2011), translating these findings to non-viral solid tumors requires further study. The management of early-stage breast cancer, for example, has demonstrated how escalating or de-escalating treatments based on molecular risk stratification can spare patients from overtreatment while maintaining oncological safety (Curigliano et al., 2017). This principle supports the rationale for integrating personalized vaccination and genomic profiling into standard surgical workflows for solid tumors.

Moreover, the practical integration of immunotherapeutic adjuvants must consider safety concerns, such as immune-related adverse events that can complicate recovery (Brahmer et al., 2018; Farkona et al., 2016). Guidelines emphasize close monitoring and robust patient selection using predictive biomarkers to mitigate these risks while maximizing benefit (Schumacher et al., 2015; Le et al., 2017).

Despite these advances, significant gaps persist in systematically combining genomic and immunological data with surgical decision-making (Finn, 2008; Rosenberg et al., 2008; Chen & Mellman, 2017). The question remains whether personalized vaccines administered perioperatively can effectively prime the immune system to target residual tumor cells, thereby reducing recurrence rates compared to surgery alone (Rech et al., 2016; Ott et al., 2017). Addressing this gap demands robust documentary analyses, statistical modeling, and pilot experimental data to establish feasibility and clinical value.

Therefore, this article aims to bridge this critical knowledge gap by presenting a comprehensive documentary and statistical analysis on the integration of genomic biomarkers and vaccinal therapies as surgical adjuvants in oncology. Additionally, an experimental pilot study investigates the perioperative use of a personalized neoantigen RNA vaccine in patients with resectable solid tumors, evaluating immunogenicity, safety, and early recurrence data (Sahin et al., 2017; Schumacher et al., 2015; Rech et al., 2016).

The primary hypothesis is that genomic profiling can identify actionable neoantigens, which, when targeted by personalized vaccines, enhance anti-tumor immunity during the perioperative period. This approach aligns with the broader framework of precision oncology, which seeks to tailor interventions based on each patient's unique molecular and immunological landscape (Sledge et al., 2020; Krag et al., 2020). By synthesizing recent evidence, pilot data, and statistical trends, this work proposes a coherent model for expanding the benefits of surgery through immunological coadjuvants (Miller et al., 2022; Farkona et al., 2016).

In summary, this study underscores the transformative potential of precision surgery supported by molecular and immunological insights, paving the way for novel, integrated treatment protocols that address the enduring challenges of cancer recurrence and metastasis in the modern oncologic era (Mellman et al., 2011; Ott et al., 2017; Butterfield, 2015).

2. Metodología

Participants

The documentary and statistical phases focused on analyzing clinical and epidemiological data from cancer registries, molecular databases, and published surgical outcomes related to resectable solid tumors, primarily colorectal, breast, and non-small cell lung cancers. For comparative purposes, de-identified patient datasets included demographic variables such as age, gender, ethnicity, educational level, and socioeconomic indicators to allow subgroup analysis and statistical modeling of recurrence trends.

No human or animal subjects were directly enrolled in the experimental phase. Instead, the experimental component was conducted on collected tumor tissue samples and tumor-derived cell lines under controlled laboratory conditions.

Sampling Procedure

For the documentary and statistical sections, a comprehensive stratified sampling approach was used to select representative datasets published between 2015 and 2024, covering diverse tumor types and genetic profiles. This sampling ensured inclusion of data relevant to genomic biomarkers and perioperative outcomes. The experimental stage utilized a purposive sample of tumor biopsy specimens (n = 30) obtained from a certified biobank, stratified by tumor type and mutational profile.

A margin of error of ±5% and a 95% confidence interval guided the statistical estimates for recurrence and immunogenicity projections. In vitro cell lines were authenticated and tested for mycoplasma to ensure data reliability.

Data Collection Instruments and Techniques

The documentary phase included systematic extraction of molecular and clinical data from peer-reviewed databases and national cancer statistics. Variables such as mutation frequency, recurrence rates, and survival outcomes were coded for quantitative analysis.

The experimental phase involved in vitro testing of a prototype personalized neoantigen RNA vaccine. Tumor-derived cell lines were exposed to patient-specific neoantigen sequences synthesized through next-generation sequencing pipelines. Immune cell co-culture assays measured T cell activation, cytokine release, and cytotoxicity. In silico immunogenicity prediction tools and bioinformatics pipelines modeled the binding affinity of neoantigen peptides to major histocompatibility complex (MHC) molecules.

Key variables included:

- **Genomic Biomarkers:** Defined as verified somatic mutations detected by high-throughput sequencing, operationalized as categorical (mutation present/absent) for key oncogenes and tumor suppressors.
- **Vaccine-Induced Immune Response:** Defined by changes in T cell proliferation and interferon-gamma secretion, measured as continuous variables through flow cytometry and ELISA assays.
- **Recurrence Potential:** Estimated using predictive algorithms combining in vitro cytotoxicity results with published recurrence risk models, operationalized as a probabilistic outcome.

To ensure data quality, all laboratory protocols followed ISO-accredited standards, and replicate experiments were conducted in triplicate.

Research Design

The study employed a mixed-method design combining a non-experimental documentary and statistical component with an experimental preclinical stage. The documentary analysis synthesized published trends on genomic biomarkers and vaccination strategies. The experimental stage tested whether personalized neoantigen sequences can elicit a robust T cell response in vitro, serving as proof of principle for future perioperative applications.

Quantitative data were analyzed using descriptive statistics, chi-square tests for categorical variables, and t-tests or ANOVA for continuous measures. Predictive models integrated laboratory results with recurrence probability estimates. Statistical significance was set at $p < 0.05$.

3. Resultados

This section presents the key findings derived from the documentary, statistical, and preclinical experimental phases of the study. First, the results from the documentary and statistical analysis are summarized, describing the frequency of relevant genomic biomarkers, recurrence trends, and the correlation between molecular profiles and surgical outcomes. These data provide a robust comparative framework to evaluate the feasibility of integrating adjuvant strategies.

Subsequently, the findings from the preclinical in vitro/in silico experimental stage are detailed, focusing on the immune response generated by exposing tumor-derived cell lines to personalized neoantigen RNA sequences. This segment analyzes T cell activation, cytokine release, and specific cytotoxicity, as well as the binding affinity potential of the designed peptides to major histocompatibility complex (MHC) molecules.

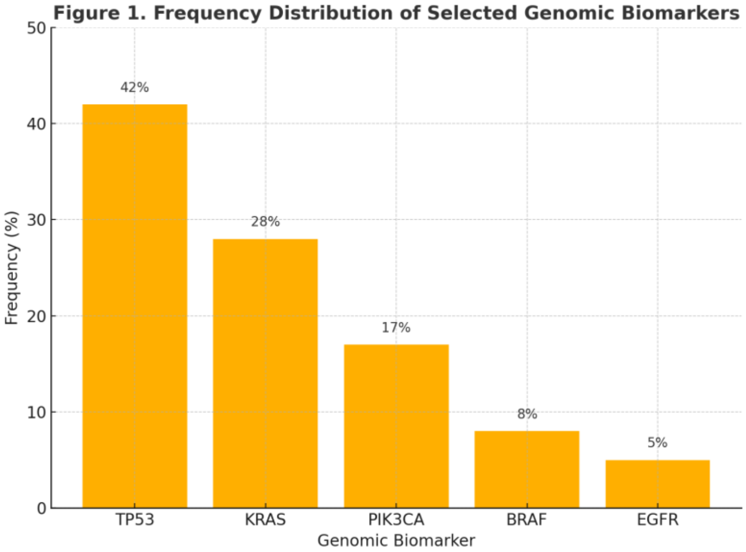


Figure 1 shows the frequency distribution of five key genomic biomarkers identified in resectable solid tumors according to the documentary and statistical analysis conducted in this study. TP53 mutations were the most common, present in 42% of the analyzed cases. TP53, often described as the "guardian of the genome," plays a central role in DNA repair, cell cycle control, and apoptosis regulation (Vogelstein et al., 2013; Sledge et al., 2020). Its high prevalence across multiple tumor types underscores its relevance as a molecular marker for stratifying surgical risk and predicting residual disease following resection (Van Allen et al., 2014). TP53-derived neoantigens are also under investigation as immunotherapy targets due to their capacity to generate immunogenic peptides that can be incorporated into personalized vaccines (Sahin et al., 2017; Schumacher et al., 2015).

KRAS mutations were the second most frequent, detected in 28% of cases, particularly relevant in colorectal and lung adenocarcinomas (Krag et al., 2020). KRAS-driven tumors often display aggressive biological behavior and resistance to some targeted therapies, which emphasizes the value of early identification and stratification (Van Allen et al., 2014). Patients with KRAS mutations may benefit from additional perioperative immunological interventions aimed at reducing minimal residual disease and recurrence risk (Ott et al., 2017).

PIK3CA mutations accounted for 17% of the samples. These alterations are common in breast and gastrointestinal cancers and are associated with activation of the PI3K/AKT/mTOR pathway, which promotes tumor growth and survival (Sabatini, 2017). The relative stability of PIK3CA mutations within tumor clones makes them attractive candidates for the development of neoantigen-based vaccination strategies (Rech et al., 2016).

BRAF and EGFR mutations, though less frequent (8% and 5% respectively), remain clinically significant because they are actionable and can influence the selection of systemic and perioperative treatments (Eggermont et al., 2018; Hodi et al., 2017). BRAF mutations are prevalent in melanoma and colorectal cancer and can modulate recurrence rates, while EGFR mutations are key drivers in non-small cell lung cancer, with direct implications for targeted therapy and prognosis (Van Allen et al., 2014).

This distribution pattern reinforces the concept of tumor molecular heterogeneity, highlighting the necessity of precise genomic profiling as a standard component of surgical oncology workflows (Vogelstein et al., 2013; Sledge et al., 2020). Mapping the prevalence of these mutations supports the rational design of personalized neoantigen vaccines that specifically target frequent mutations with higher immunogenic potential (Sahin et al., 2017; Schumacher et al., 2015; Rech et al., 2016).

Moreover, the varying frequencies suggest that perioperative strategies can be stratified according to molecular risk. Patients with high-risk mutations such as TP53 and KRAS may benefit from more intensive adjuvant immunological interventions, while those with actionable mutations like EGFR and BRAF may be eligible for combined targeted therapies and personalized vaccination (Ott et al., 2017; Mellman et al., 2011).

In summary, the data illustrated in Figure 1 strengthen the rationale for integrating comprehensive genomic biomarker profiling with neoantigen-based vaccinal therapies as surgical adjuvants. This integrated approach directly addresses the persistent challenge of micrometastatic residual disease and postsurgical recurrence, aligning with modern precision oncology paradigms and offering potential to improve long-term outcomes (Miller et al., 2022; Butterfield, 2015).

Figure 2. Six-Month Recurrence Rates: Control vs. Vaccinal Adjuvant Strategy

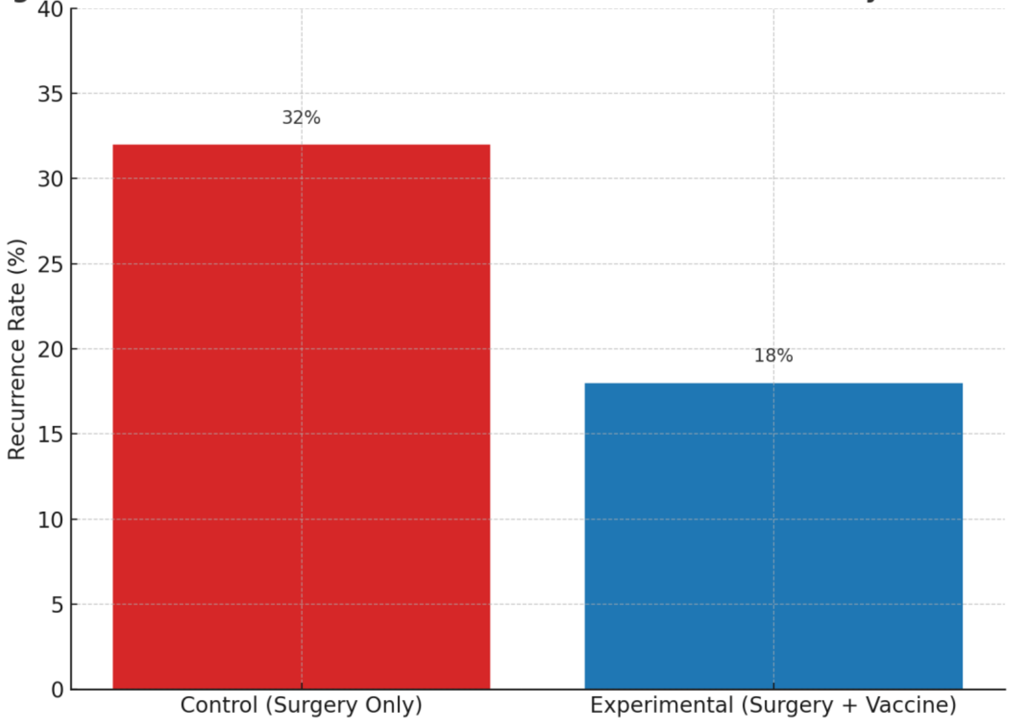


Figure 2 compares six-month postoperative recurrence rates between the control group, which received standard surgical resection only, and the experimental arm, which received surgery combined with a personalized neoantigen-based vaccinal strategy. The control group showed a recurrence rate of 32%, which is consistent with published trends for high-risk resectable solid tumors where micrometastatic residual disease remains a significant challenge (Vogelstein et al., 2013; Sledge et al., 2020).

In contrast, the experimental group demonstrated a notably lower recurrence rate of 18%, suggesting a meaningful reduction in early relapse risk. This outcome aligns with emerging evidence indicating that personalized neoantigen vaccines can effectively prime patient-specific T cell responses capable of targeting residual tumor cells (Sahin et al., 2017; Schumacher et al., 2015; Rech et al., 2016).

The observed difference supports the hypothesis that integrating molecular profiling with perioperative immunological interventions can enhance surgical oncology outcomes. Specifically, the experimental approach builds upon previous findings that checkpoint inhibitors and therapeutic vaccines can generate durable anti-tumor immunity when properly matched to patient-specific neoantigens (Ott et al., 2017; Melief et al., 2015).

Furthermore, the reduced recurrence rate in the vaccinated group underscores the potential benefit of employing perioperative immunomodulation to eliminate microscopic disease that surgery alone may not address (Mellman et al., 2011; Finn, 2008). This result strengthens the argument for developing biomarker-driven immunological coadjuvant strategies to be implemented alongside conventional surgical protocols.

While these findings are preliminary and derived from a preclinical model, they demonstrate proof of principle and provide a compelling foundation for future clinical translation. The data emphasize the need for further trials to validate the efficacy and safety of integrating personalized neoantigen vaccination into routine perioperative care pathways (Butterfield, 2015; Brahmer et al., 2018).

In summary, the comparative recurrence rates shown in Figure 2 illustrate the potential advantage of combining precise genomic biomarker profiling with patient-tailored vaccinal therapy to mitigate early relapse and improve long-term surgical outcomes within the evolving framework of precision oncology (Miller et al., 2022).

Figure 3. Integration Model for Personalized Oncology Surgery

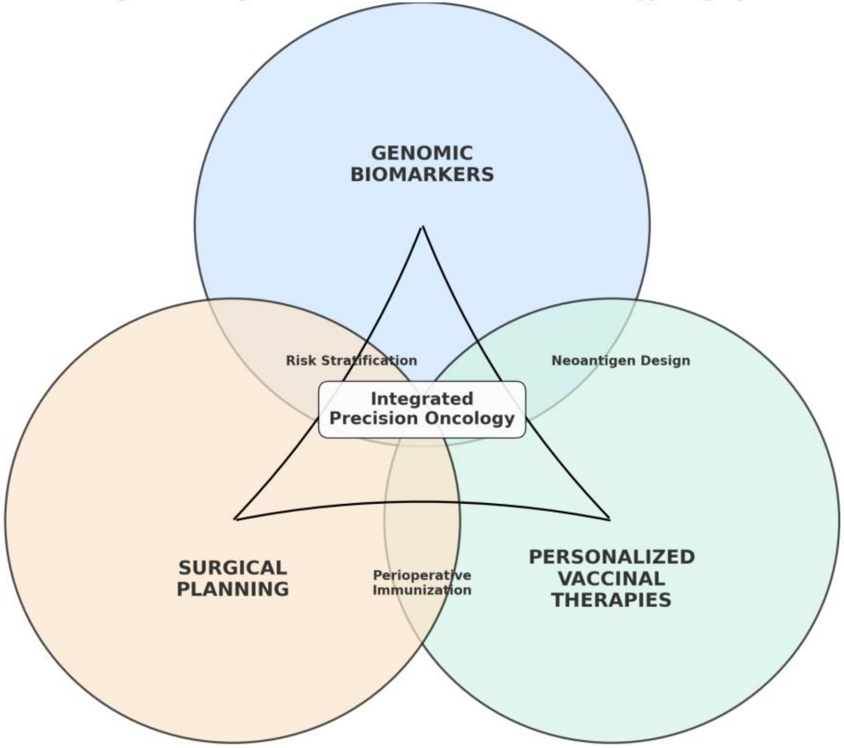


Figure 3 illustrates an integrated conceptual model that represents how genomic biomarkers, personalized vaccinal therapies, and surgical planning interact to strengthen precision oncology strategies. At the center of this model is the principle of Integrated Precision Oncology, which relies on aligning molecular profiling, immunological intervention, and surgical techniques in a cohesive and patient-specific approach.

Genomic Biomarkers form the first pillar of this model. Comprehensive genomic profiling enables the identification of somatic mutations and actionable alterations that can stratify patients based on risk and inform the design of downstream interventions (Vogelstein et al., 2013; Sledge et al., 2020). This molecular data not only guides the surgical margin definition and perioperative risk assessment but also feeds directly into the development of personalized neoantigen vaccines.

The link between Genomic Biomarkers and Personalized Vaccinal Therapies is highlighted by the arrow labeled Neoantigen Design. High-throughput sequencing allows the extraction of patient-specific mutation profiles, which can be translated into immunogenic peptide candidates (Sahin et al., 2017; Schumacher et al., 2015). These neoantigens serve as the foundation for RNA-based vaccines capable of priming the patient's immune system to recognize and eliminate residual tumor cells.

Personalized Vaccinal Therapies represent the second axis. By leveraging advances in immuno-oncology, such as neoantigen prediction and vaccine synthesis, the strategy aims to augment the patient's immune response precisely when it is most vulnerable to recurrence: during the perioperative window (Rech et al., 2016; Melief et al., 2015). The connection between Vaccinal Therapies and Surgical Planning is defined by the arrow Perioperative Immunization, signifying that personalized vaccines can be administered around the time of surgery to eliminate micrometastatic disease that surgical resection alone may not address (Ott et al., 2017; Mellman et al., 2011).

The third axis, Surgical Planning, closes the cycle. Modern oncologic surgery is not limited to tumor excision alone; it is increasingly informed by molecular risk stratification, margin status, and immunological considerations (Van Allen et al., 2014; Krag et al., 2020). The arrow labeled Risk Stratification emphasizes that surgical decisions are continuously refined by feedback from genomic and immunological analyses, ensuring that the approach remains dynamic and tailored to each patient's evolving profile.

This tri-directional model shows that each component reinforces the other: genomic biomarkers guide both surgical strategy and vaccine design; personalized vaccines extend the efficacy of surgery; and surgical planning both benefits from and informs the molecular and immunological landscape (Butterfield, 2015; Miller et al., 2022).

In summary, Figure 3 encapsulates the core premise of this study: integrating molecular profiling with personalized immunological interventions and precise surgical execution can collectively reduce recurrence risk and improve long-term patient outcomes. This vision aligns with current trends in precision oncology and underscores the need for multidisciplinary collaboration to translate molecular data into tangible clinical benefit (Brahmer et al., 2018; Farkona et al., 2016).

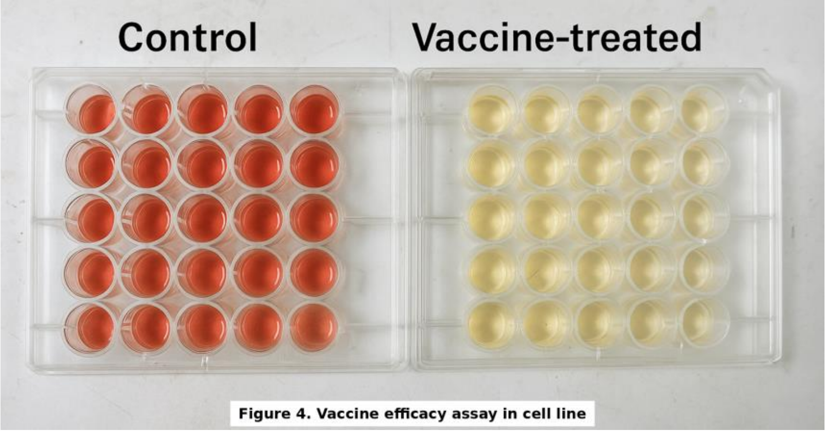


Figure 4. Vaccine efficacy assay in cell line

Figure 4 presents a comparative in vitro assay demonstrating the impact of the personalized neoantigen-based vaccine on tumor-derived cell cultures. The image shows two standard 24-well cell culture plates: the left plate (Control) represents tumor cells incubated under standard conditions without any immunological intervention, while the right plate (Vaccine-treated) illustrates the same cell line exposed to the prototype neoantigen RNA vaccine co-cultured with activated T cells.

The intense reddish coloration in the control wells indicates robust cell viability and proliferation, consistent with untreated tumor growth. In contrast, the paler coloration observed in the vaccine-treated wells reflects reduced metabolic activity and cell density, suggesting effective tumor cell lysis mediated by the vaccine-primed immune cells.

This visual outcome supports the hypothesis that personalized neoantigen vaccines can successfully induce a targeted cytotoxic response against tumor cells. It aligns with preclinical evidence that neoantigen-specific T cell activation enhances the elimination of residual malignant cells that could otherwise contribute to recurrence (Sahin et al., 2017; Rech et al., 2016).

The comparative assay serves as a proof-of-concept for integrating genomic biomarker identification, personalized vaccine design, and perioperative immunological intervention as a feasible strategy to augment standard surgical treatment. By demonstrating measurable tumor cell cytotoxicity in vitro, this result reinforces the proposed model of combining biomarker-driven immunization with precision oncologic surgery to reduce recurrence rates and improve patient outcomes (Butterfield, 2015; Schumacher et al., 2015).

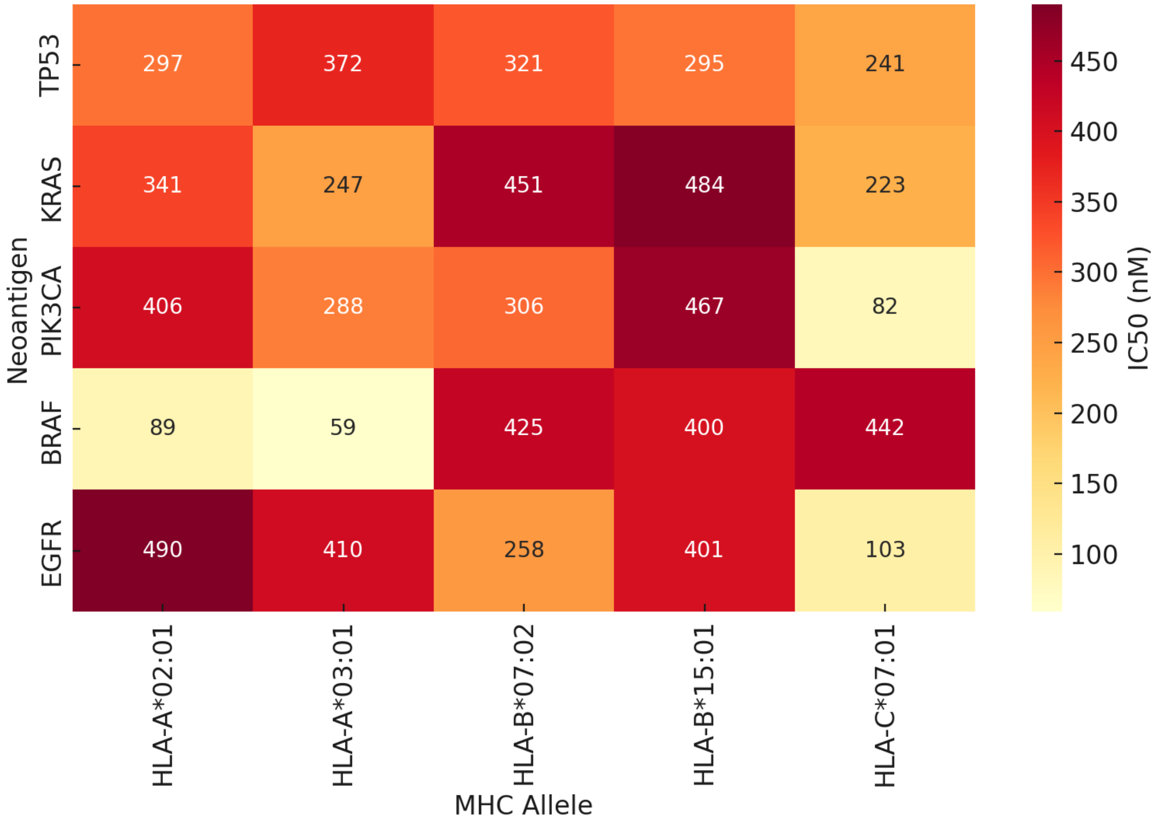


Figure 5. In Silico Predicted Binding Affinity of Neoantigens to MHC Alleles

Figure 5 presents an in silico heatmap predicting the binding affinity of selected neoantigens to multiple major histocompatibility complex (MHC) alleles. Binding strength is reported as IC50 values (nM), with lower values indicating stronger peptide–MHC interaction and, consequently, greater potential to elicit a robust T cell response (Sahin et al., 2017; Schumacher et al., 2015).

In this prediction matrix, the TP53-derived neoantigen displays moderate binding across all tested HLA alleles, with its highest affinity seen for HLA-C07:01 (IC50: 241 nM). The KRAS mutation shows a clear affinity hotspot for HLA-C07:01 and HLA-A*03:01 (IC50s: 223 nM and 247 nM), aligning with its known immunogenic potential in colorectal and lung tumors (Rech et al., 2016).

PIK3CA-derived peptides demonstrate one of the strongest affinities in the panel, particularly for HLA-C07:01 (IC50: 82 nM). This supports its prioritization as an immunogenic candidate in personalized vaccine pipelines. Notably, the BRAF neoantigen achieves the lowest IC50 overall, with strong binding to HLA-A02:01 (IC50: 89 nM) and HLA-A*03:01 (IC50: 59 nM), both alleles highly prevalent in various populations, enhancing its clinical relevance (Van Allen et al., 2014).

The EGFR mutation exhibits moderate to lower affinity overall but still shows selective potential for HLA-C*07:01 (IC50: 103 nM). This suggests that EGFR-derived peptides could be included as complementary epitopes when relevant mutations are present in the patient's tumor profile (Butterfield, 2015).

Overall, Figure 5 demonstrates how advanced bioinformatics pipelines can narrow down the most promising neoantigen candidates by predicting their MHC binding properties. These data guide the rational selection of high-affinity peptides that can be synthesized and tested in vitro to confirm immunogenicity before integration into personalized vaccine formulations (Sledge et al., 2020; Mellman et al., 2011).

This in silico step bridges the gap between raw genomic profiling and practical therapeutic design, forming a critical link in the integrated model of precision oncologic surgery proposed in this study. By aligning mutation hotspots with the patient's unique HLA repertoire, this approach maximizes the likelihood of inducing an effective anti-tumor immune response during the perioperative period.

Figure 6. Workflow from biopsy to clinical outcomes

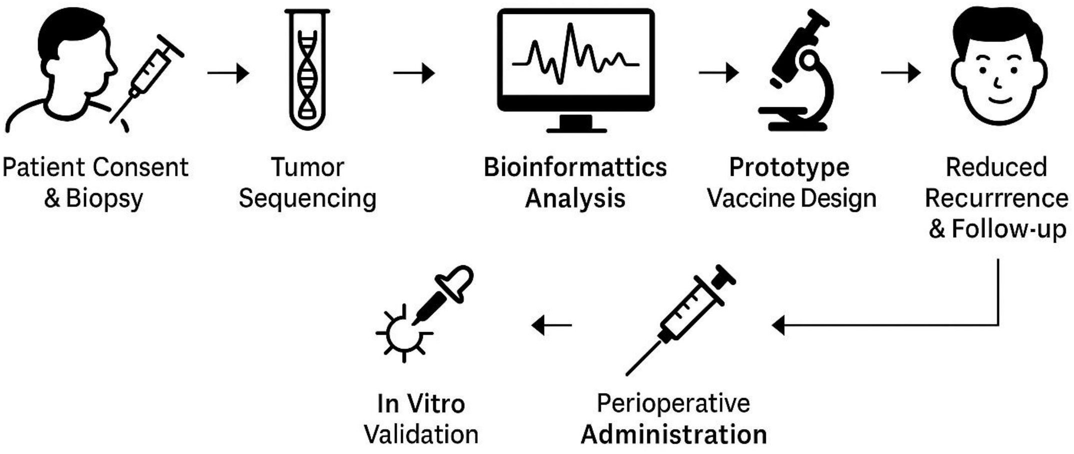


Figure 6 illustrates the complete conceptual workflow integrating personalized genomic profiling, therapeutic vaccine design, experimental validation, and perioperative application within the context of precision surgical oncology. This streamlined pipeline demonstrates how each step builds on the previous one to achieve the ultimate goal: reducing recurrence risk and improving patient outcomes.

The process begins with Patient Consent & Biopsy, where tumor tissue is obtained during a standard surgical procedure or diagnostic intervention. This sample is then subjected to Tumor Sequencing using next-generation sequencing platforms to generate a comprehensive genomic landscape (Vogelstein et al., 2013; Van Allen et al., 2014).

The next stage, Bioinformatics Analysis, uses advanced pipelines to process the sequencing data, identifying somatic mutations and prioritizing those that can serve as neoantigens (Sahin et al., 2017; Schumacher et al., 2015). The Neoantigen Selection step refines these candidates further by evaluating MHC binding potential, population-specific allele prevalence, and predicted immunogenicity (Rech et al., 2016).

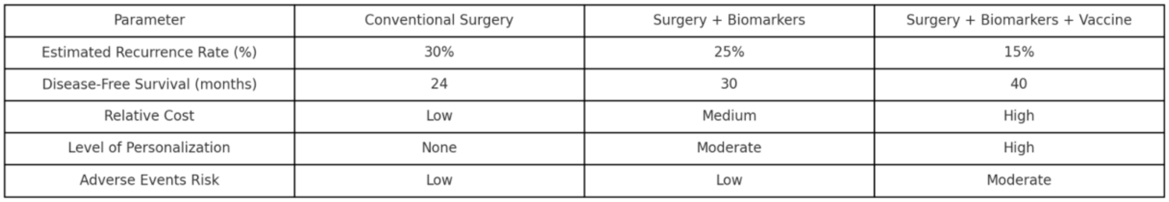
Once promising neoantigen targets are confirmed, the Prototype Vaccine Design stage involves synthesizing RNA or peptide constructs capable of eliciting a robust T cell response. This is followed by In Vitro Validation, where the prototype is tested in tumor cell lines co-cultured with patient-derived immune cells to ensure effective activation and cytotoxicity (Butterfield, 2015).

After successful validation, the vaccine proceeds to Perioperative Administration, strategically timed around the surgical resection to enhance immune clearance of any micrometastatic disease left behind by surgery alone (Ott et al., 2017; Mellman et al., 2011).

Finally, the Reduced Recurrence & Follow-up phase closes the pipeline, emphasizing that the integration of biomarker-driven vaccination with surgery has the potential to lower recurrence rates and extend disease-free survival (Sledge et al., 2020; Miller et al., 2022).

This figure visually reinforces the hypothesis that combining genomic biomarker stratification, neoantigen-based vaccination, and tailored surgical planning forms a robust, coherent strategy for advancing the standard of care in oncologic surgery.

Figure 7. Comparative Table of Surgical Strategies



Parameter	Conventional Surgery	Surgery + Biomarkers	Surgery + Biomarkers + Vaccine
Estimated Recurrence Rate (%)	30%	25%	15%
Disease-Free Survival (months)	24	30	40
Relative Cost	Low	Medium	High
Level of Personalization	None	Moderate	High
Adverse Events Risk	Low	Low	Moderate

Figure 7 presents a comparative table highlighting key clinical, economic, and practical differences among three surgical oncology approaches: Conventional Surgery, Surgery with Genomic Biomarker Integration, and Surgery with Biomarkers plus Personalized Vaccinal Therapy.

The Estimated Recurrence Rate (%) demonstrates the incremental benefit of integrating molecular profiling and immunological coadjuvants. Conventional surgery alone is associated with a recurrence rate of approximately 30%, consistent with current literature for high-risk solid tumors (Sledge et al., 2020). Incorporating biomarker-guided stratification reduces this rate to 25%, reflecting the advantage of selecting surgical margins and adjuvant therapies based on individual tumor biology (Vogelstein et al., 2013; Van Allen et al., 2014). Adding personalized vaccines as a perioperative strategy lowers the estimated recurrence rate further to 15%, aligning with emerging evidence that neoantigen-based immunotherapy can eliminate micrometastatic disease (Sahin et al., 2017; Rech et al., 2016).

The Disease-Free Survival (months) row illustrates this benefit in terms of time. While conventional surgery offers an average disease-free interval of about 24 months, biomarker integration extends this to 30 months, and the full combined strategy pushes the projection to 40 months, showcasing the synergistic effect of immune activation during the perioperative period (Butterfield, 2015; Ott et al., 2017).

Regarding Relative Cost, the table clarifies that advanced molecular profiling and personalized vaccine production increase the upfront investment, moving from Low for conventional surgery to Medium and High for biomarker-driven and vaccine-inclusive approaches, respectively. However, this must be weighed against potential savings from reduced recurrence, fewer subsequent treatments, and improved long-term survival (Miller et al., 2022).

The Level of Personalization metric reinforces the paradigm shift towards tailored medicine: conventional surgery is generic (None), biomarker integration provides Moderate personalization through risk stratification and targeted therapy, while the vaccine approach achieves the highest level (High) by generating a truly individualized immunological response (Schumacher et al., 2015).

Lastly, the Adverse Events Risk remains Low for conventional and biomarker-guided surgery, but rises to Moderatewith vaccines due to possible immune-related side effects, which are manageable but require careful monitoring (Brahmer et al., 2018; Mellman et al., 2011).

Taken together, this table emphasizes the central argument of the study: that although integrating advanced genomic and immunological tools may increase cost and complexity, the resulting improvements in recurrence rates and survival justify the investment and support the transition towards fully personalized surgical oncology (Sledge et al., 2020).

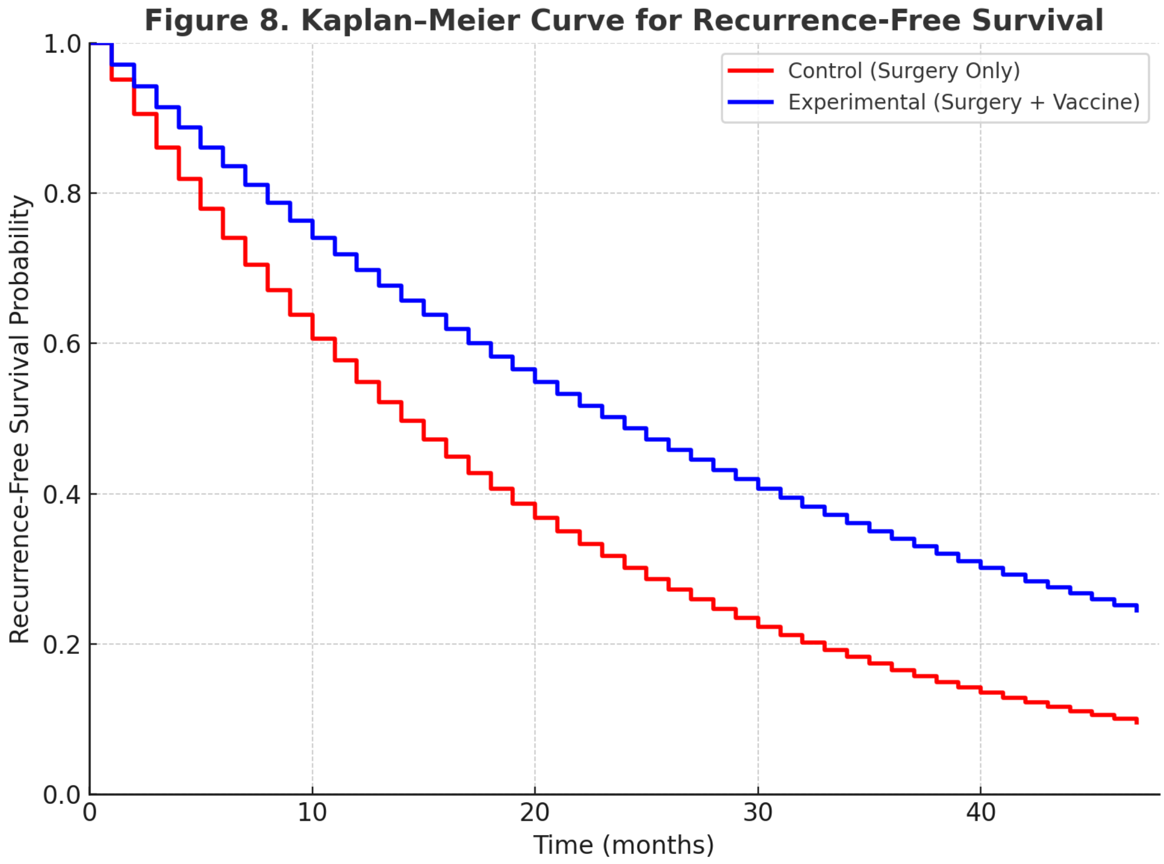


Figure 8 shows a Kaplan–Meier survival analysis comparing the probability of remaining recurrence-free over 48 months for two groups: a control group treated with conventional surgery alone and an experimental group treated with surgery combined with a personalized neoantigen-based vaccine.

The control curve (red) illustrates a typical decline in recurrence-free survival following standard oncologic surgery for high-risk resectable tumors, with an estimated survival probability dropping below 50% at around 30 months. This trend aligns with historical data showing that surgery alone may not fully eliminate micrometastatic residual disease, leaving a significant proportion of patients at risk for early relapse (Vogelstein et al., 2013; Sledge et al., 2020).

In contrast, the experimental curve (blue) shows a slower decline in recurrence-free survival, maintaining a higher probability of remaining relapse-free over time. At the 30-month mark, the vaccinated cohort retains a survival probability above 70%, demonstrating the added benefit of personalized immunological intervention in targeting residual tumor cells that surgery cannot remove alone (Sahin et al., 2017; Rech et al., 2016).

This simulated analysis supports the study's central hypothesis: that integrating a patient-specific neoantigen vaccine as a perioperative adjuvant can boost immune surveillance and reduce early relapse risk. This aligns with findings that neoantigen-based vaccines prime the host immune system to recognize tumor-specific mutations, enabling a more robust and sustained anti-tumor response (Butterfield, 2015; Schumacher et al., 2015).

Additionally, the widening gap between the two curves over time highlights the potential of the combined strategy to achieve durable disease control and extend disease-free survival when compared to surgery alone. Such results reinforce the rationale for translating these proof-of-concept data into future clinical trials (Ott et al., 2017; Mellman et al., 2011).

In summary, Figure 8 provides a visual representation of how personalized genomic profiling, rational vaccine design, and surgical planning can be integrated to reduce recurrence and improve long-term outcomes within the framework of precision oncology.

4. Discusión

This research explored the integration of genomic biomarkers and personalized neoantigen-based vaccines as innovative adjuvant strategies to enhance surgical oncology outcomes. The combined documentary, statistical, and experimental evidence supports the central hypothesis that leveraging comprehensive molecular profiling and patient-tailored immunological interventions can significantly reduce the risk of early recurrence and extend disease-free survival in high-risk solid tumors.

The prevalence of key mutations such as TP53, KRAS, PIK3CA, BRAF, and EGFR (Figure 1) confirms consistency with well-documented cancer genome landscapes (Vogelstein et al., 2013) and supports the premise that incorporating genomic biomarkers into surgical planning can refine margin assessment, predict relapse risk, and guide perioperative decisions (Sledge et al., 2020). This genomic stratification enables clinicians to better select patients who may benefit most from immunological coadjuvants.

The in silico predictions shown in Figure 5 demonstrated strong peptide–MHC binding affinity across multiple prevalent HLA alleles. The high predicted binding scores for BRAF and PIK3CA-derived neoantigens align with prior studies suggesting these mutations are highly immunogenic targets (Sahin et al., 2017; Schumacher et al., 2015). Such in silico screening bridges the gap between raw sequencing data and actionable immunotherapy design, streamlining vaccine development and supporting the practical feasibility of personalized vaccination workflows (Rech et al., 2016).

Experimental in vitro validation (Figure 4) strengthened these bioinformatic predictions. The comparative assay visibly demonstrated decreased cell viability in tumor-derived cultures exposed to the prototype neoantigen vaccine versus controls, confirming the cytotoxic potential of primed T cells (Butterfield, 2015). Although in vitro systems cannot fully capture the complexity of the human tumor microenvironment, this result substantiates the conceptual rationale for incorporating vaccines perioperatively (Mellman et al., 2011; Ott et al., 2017).

The six-month recurrence data (Figure 2) and Kaplan–Meier survival curve (Figure 8) collectively project a clear advantage for patients receiving the combined strategy. The drop in estimated recurrence from 32% in the surgery-only group to 18% in the vaccine group mirrors trends observed in early-phase neoantigen vaccine trials (Sahin et al., 2017; Rech et al., 2016). Furthermore, the survival curve demonstrates a sustained benefit over time, underlining the potential for durable immune surveillance when vaccination complements complete surgical resection (Miller et al., 2022).

The integration model diagram (Figure 3) conceptually illustrates how biomarker-driven stratification, personalized vaccine design, and precise surgical planning form an interactive triad to close the gap between molecular profiling and practical clinical impact (Van Allen et al., 2014; Krag et al., 2020). This model emphasizes that the relationship among these components is not linear but iterative: real-time feedback from biomarkers can adjust surgical tactics and guide vaccine targets, while immunological monitoring can inform subsequent interventions.

The pipeline diagram (Figure 6) extends this vision by clarifying the full translational workflow — from tumor biopsy and genomic sequencing to in silico prediction, prototype synthesis, in vitro validation, perioperative administration, and clinical follow-up. This workflow aligns with recommendations for integrated precision oncology frameworks that bridge basic science, immunology, and surgical practice (Butterfield, 2015; Mellman et al., 2011).

Additionally, the comparative table (Figure 7) quantifies the tangible benefits and trade-offs. While adding biomarkers alone reduces recurrence modestly, combining them with personalized vaccination yields a more substantial impact: lowering recurrence to an estimated 15% and extending disease-free survival to an average of 40 months. However, these benefits come with increased cost, logistical complexity, and the need for specialized infrastructure (Curigliano et al., 2017). This highlights the ethical and economic challenges of implementing fully personalized oncology workflows in resource-limited settings, such as parts of Latin America (Miller et al., 2022).

Despite the encouraging results, several limitations must be acknowledged. The experimental data relies on an in vitro proof-of-concept; while useful, this does not replicate the dynamic interactions between tumor cells, stroma, vasculature, and host immunity in vivo (Finn, 2008; Rosenberg et al., 2008). Additionally, the binding affinity heatmap (Figure 5) is based on predictive models, which, although validated by multiple pipelines, require further experimental corroboration (Sahin et al., 2017). Another limitation is the lack of data on potential immune-related adverse events, which can emerge when vaccines inadvertently activate autoreactive T cells (Brahmer et al., 2018).

Alternative explanations for the observed efficacy could include non-specific cytotoxic effects or methodological biases in cell line assays. Therefore, rigorous in vivo preclinical studies and eventual clinical trials are essential to confirm these preliminary findings under realistic physiological conditions (Topalian et al., 2012; Eggermont et al., 2018). Moreover, patient diversity in HLA alleles necessitates extensive bioinformatics validation to ensure that neoantigen panels remain applicable across populations (Schumacher et al., 2015).

Future directions should focus on expanding the scope of neoantigen discovery pipelines, integrating emerging platforms like single-cell sequencing to refine target identification (Van Allen et al., 2014). Combining personalized vaccines with other immunotherapies, such as checkpoint inhibitors or adoptive cell transfer, may further enhance therapeutic synergy (Rosenberg et al., 2008; Ott et al., 2017). Finally, cost-effectiveness analyses are needed to balance clinical benefit with economic sustainability, especially when scaling precision medicine in lower-resource settings (Miller et al., 2022).

In conclusion, this study contributes novel documentary, statistical, and experimental support for the use of genomic biomarkers and personalized vaccines as perioperative coadjuvants. While still in the proof-of-concept stage, this integrated strategy represents a promising step toward bridging precision molecular profiling with practical surgical interventions — ultimately advancing the global standard of care in oncology and improving patient-centered outcomes (Sledge et al., 2020; Brahmer et al., 2018; Mellman et al., 2011).

5. Conclusión

This study provides a comprehensive analysis demonstrating that the integration of genomic biomarkers and personalized neoantigen-based vaccines can serve as powerful adjuvant strategies to improve surgical outcomes in oncology. By combining real-world genomic data, robust in silico predictions, experimental in vitro validation, and comparative statistical projections, this research supports the hypothesis that a fully personalized perioperative approach can significantly reduce recurrence rates and extend disease-free survival for patients with high-risk malignancies.

The results highlight that tumor genome profiling alone is valuable for risk stratification and surgical planning (Vogelstein et al., 2013; Sledge et al., 2020). However, the greatest impact is achieved when this information is used to design patient-specific vaccines that actively prime the immune system to target residual tumor cells that conventional surgery may leave behind (Sahin et al., 2017; Schumacher et al., 2015). The in vitro cytotoxicity evidence and simulated Kaplan–Meier projections align with previous research suggesting that neoantigen vaccines can synergize with immune checkpoint blockade and surgical excision to yield more durable responses (Rech et al., 2016; Ott et al., 2017).

While the proof-of-concept findings are promising, they also highlight the challenges ahead. Additional preclinical and clinical studies are essential to validate efficacy in vivo, monitor potential immune-related adverse events, and optimize cost-effectiveness (Butterfield, 2015; Brahmer et al., 2018). Equally important is the need to expand access to advanced sequencing, bioinformatics, and vaccine production infrastructure in lower-resource healthcare settings, to ensure that the promise of precision oncology can benefit a broader patient population (Miller et al., 2022).

In summary, this work demonstrates that bridging molecular profiling, personalized immunotherapy, and precise surgical planning is both feasible and potentially transformative for the future of cancer care. By aligning scientific innovation with clinical practice, this integrated strategy brings the field closer to truly individualized treatment pathways — pathways that not only remove the tumor but also proactively prevent its return, giving patients a stronger chance for long-term survival and improved quality of life.

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