MINI REVIEW
Iran J Allergy Asthma Immunol
In press.

Neoantigens in Cancer Immunotherapy: An Overview with a Focus on Non-small Cell Lung Cancer and Pancreatic Ductal Adenocarcinoma

Fatemeh Eskandari-Malayeri[1], Sajjad shekarchian[1], and Esmail Mortaz[1,2]

[1] Department of Immunology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2] Respiratory Immunology Center, National Research Institute of Tuberculosis and Lung Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Received: 6 July 2025; Received in revised form: 20 September 2025; Accepted: 10 November 2025

ABSTRACT

Non-small cell lung cancer (NSCLC) and pancreatic ductal adenocarcinoma (PDAC) figure prominently in the list of prevalent and resistant cancers that reveal significant differences in response to immunotherapy. Neoantigens, specific antigens resulting from tumor mutations, play an important role in provoking immune responses and the success of immunotherapy. This review scrutinizes the quantitative and qualitative differences in neoantigens in NSCLC and PDAC and their impact on the efficacy of immunotherapy. The evidence suggests that the higher mutational burden, greater diversity, and different quality of neoantigens in NSCLC compared with PDAC are among the key drivers contributing to the enhanced susceptibility to immunotherapy in this cancer. These differences could pave the way for the development of personalized therapies and novel strategies to improve treatment outcomes in resistant cancers.

Keywords: Cancer immunotherapy; Non-small cell lung cancer; Neoantigens; Pancreatic ductal adenocarcinoma

INTRODUCTION

Cancer persists as a globally paramount public health issue, annually affecting millions of individuals. The World Health Organization's 2022 estimates, which documented approximately 20 million new diagnoses and 10 million deaths, coupled with a potential escalation to over 35 million new cases annually by 2050, underscore this reality.[1] This escalating global cancer burden magnifies the need for sustained efforts in both basic biological research and the therapeutic development of novel modalities.[2–4] Among the vast range of malignant neoplasms, non-small cell lung cancer (NSCLC) and pancreatic ductal adenocarcinoma (PDAC) warrant particular scholarly and clinical attention.[5–7] This stepped-up consideration is justified by their marked incidence rates, biologically distinctive and aggressive characteristics, and the exceptionally complex therapeutic challenges they pose. Consequently, a profound and comprehensive understanding of the intricate pathobiological mechanisms underpinning these specific malignancies is an indispensable prerequisite for the rational design and successful clinical translation of effective therapeutic strategies, with a particular emphasis on pioneering immunotherapeutic approaches.[8–10]

Corresponding Author: Esmail Mortaz, PhD;
Department of Immunology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Tel: (+98 21) 2712 2275), Fax: (+98 27) 122 275, Email: emortaz@gmail.com

*The first and second authors contributed equally to this study

Published by Tehran University of Medical Sciences (http://ijaai.tums.ac.ir)

NSCLC, representing approximately 80%–85% of all lung malignancies,[11] covers three primary histopathological subtypes-adenocarcinoma, squamous cell carcinoma, and large cell carcinoma-each distinguished by unique hallmarks and differential therapeutic sensitivity.[12] Despite the fact that cigarette smoking is generally reputed to be the primary cause, adenocarcinoma, the principal histological type, often emerges in people who have always abstained from tobacco.[11] The initial clinical manifestations, often characterized by a constellation of nonspecific respiratory and systemic symptoms, including chronic cough, pleuritic discomfort, hemoptysis, cachexia, and dyspnea, commonly lead to chronologically late diagnosis and advanced-stage presentation.[11] With 5-year survival rates of roughly 64% for locoregionally confined neoplasms and only 9% for distant metastatic involvement, prognostic outcomes are significantly dependent on disease staging at diagnosis.[13] The therapeutic algorithm for NSCLC, separated based on clinically and pathobiologically stage-specific criteria, integrates surgical resection, platinum-based chemotherapy, thoracic radiotherapy, molecularly targeted agents, and, more recently, immune checkpoint inhibitors (ICIs), thereby constituting a multifaceted treatment paradigm.[14–16] The advent of ICIs, particularly in patient cohorts exhibiting elevated programmed death-ligand 1 (PD-L1) expression or tumoral mutational burden (TMB), has yielded a paradigm shift in treatment efficacy and patient quality-of-life metrics.[17,18] Furthermore, the use of neoadjuvant immunotherapeutic regimens before surgery is emerging as a popular standard-of-care strategy.[19–21]

PDAC, a malignancy originating from the pancreatic ductal epithelium, is the main and deadliest manifestation of pancreatic cancer, constituting over 80% of all identified patients.[22,23] The exceedingly poor prognosis associated with PDAC can be mostly assigned to its intrinsically and biologically complex tumor microenvironment, characterized by a dense, tissue-remodeled desmoplastic stromal reaction that impedes therapeutic intervention and promotes disease progression.[24–26] Genetic factors that contribute to the risk of PDAC encompass germline mutations in genes like *BRCA1/2* or *PALB2*. Lifestyle factors that increase the risk include smoking, being overweight, having chronic pancreatic inflammation (chronic pancreatitis), and having long-term uncontrolled diabetes.[27–29] The insidious nature of early-stage PDAC often manifests through vague and nonspecific symptomatology, such as icterus, diffuse abdominal discomfort, unintentional cachexia, and various gastrointestinal disturbances, consequently leading to diagnostic deferral in the majority of affected individuals.[30,31] Compounding these diagnostic challenges is the lack of efficacious screening modalities and the deep anatomical retroperitoneal location of the pancreas, which collectively hinder timely identification. Resultantly, a mere 15%–20% of patients present with disease amenable to surgical resection, and even among this select cohort, the postoperative recurrence rates are high.[32] The overall prognosis for PDAC is exceptionally grim, underscored by a 5-year relative survival rate reported at less than 6%.[33] In the context of advanced, unresectable disease, conventional chemotherapeutic regimens offer only palliative benefit with a limited duration of response, while the profound immunosuppressive 'cold' immune microenvironment and substantial stromal barriers contribute significantly to the observed resistance to current immunotherapeutic strategies.[34,35] These multifaceted pathobiological and clinical features collectively render PDAC one of the most formidable oncological challenges, thereby galvanizing intensive research efforts aimed at the development of novel targeted therapeutic paradigms and innovative approaches to beneficially modulate the tumor microenvironment.

In spite of paradigm-shifting progress in oncological treatment modalities, immunotherapeutic response heterogeneity remains a pervasive challenge across a world of different tumor histotypes. The deployment of ICI-based therapeutic protocols within NSCLC management has yielded substantial survival advantages and enhanced patient-reported quality-of-life indices, whereas analogous immunotherapeutic strategies in PDAC treatment frameworks have demonstrated marginal efficacy amid complex tumor microenvironment–associated resistance mechanisms.[36,37] This stark intertumoral efficacy divergence reflects the intricate tumor-specific immunobiological and molecular complexity underpinning therapeutic responsiveness and underscores the imperative for systematic delineation of cancer-specific immunotherapy response determinants.

Researchers have been investigating the role of genetic and molecular factors, especially TMB and neoantigen diversity, in the success or failure of immune-based therapies in recent years. One of the main

goals of these studies is to determine how the neoantigens in NSCLC and PDAC differ in terms of quantity and quality, and how these differences affect the immune system and the health of patients.[23,38–41] A deep understanding of these differences could lead to the creation of targeted and personalized treatments and new ways to overcome therapeutic resistance in cancers like PDAC that do not respond to treatment.

Neoantigens and Importance in Immunotherapy

Neoantigens, peptide sequences not present in the normal somatic cell repertoire, can be traced back to somatic mutations within the genome of cancer cells.[42] These genetic anomalies extend over a spectrum of alterations, including point mutations, insertions/deletions, and gene rearrangements,[43,44] which result in the synthesis of atypical proteins characterized by previously nonexistent amino acid sequences. After being broken down by proteolytic enzymes inside cancer cells, these changed proteins yield truncated peptide fragments that are then displayed on the surface of tumor cells by Major Histocompatibility Complex (MHC) class I or class II molecules.[45–48] Neoantigens manifest in two primary forms: totally tumor-specific truncal and subpopulation-specific clonal.[40,45] Truncal neoantigens, ubiquitously expressed across the entire tumor cell population due to their emergence from early oncogenic events, are highly prized targets for immunotherapy, as their engagement opens the door to the potential to eradicate a substantial proportion, if not the entirety, of the malignant cell burden. Conversely, clonal neoantigens, restricted to specific subclones as products of ongoing intratumoral heterogeneity and evolutionary divergence, may, upon targeting, contribute to partial tumor regression, with the inherent risk of immune evasion by surviving, neoantigen-deficient cell populations.[40,45,49] Owing to their ubiquitous expression in malignant cells, the peptides are recognized as immunologically non-self, particularly by cytotoxic $CD8^+$ T lymphocytes (CTLs), eliciting a robust and specific anti-tumor immune response compared with self-antigens, which are subject to immunological tolerance.[50–52] This tumor-specificity minimizes the risk of off-target effects and damage to healthy tissues, rendering them exceptionally suitable targets for personalized immunotherapeutic interventions.[53]

The clinical importance of neoantigens and their nascent therapeutic applications in cancer immunotherapy exhibits a wide array of aspects. Primarily, their non-self origin means they largely circumvent central immunological tolerance mechanisms, ensuring that T lymphocytes specific for these epitopes maintain their functional reactivity.[51,54] Second, neoantigens are important biomarkers for predicting how well patients will respond to immunotherapy. In fact, strong evidence shows that people with tumors that have a high TMB and a correspondingly high number of neoantigens have better clinical outcomes when treated with ICIs.[55,56] Furthermore, the identification and targeting of neoantigens form the basis of the development of highly personalized therapeutic vaccines, a strategy promising greater treatment efficacy alongside a minimized profile of adverse events.[57,58]

Malignancies with a high TMB, exemplified by NSCLC, typically lead to the development of a proportionately richer repertoire of neoantigens, consequently revealing enhanced sensitivity to immunotherapeutic strategies.[59–61] In such patients, this neoantigen abundance is instrumental in provoking robust anti-tumor immune surveillance and effector functions.[61] As a result, immunotherapy has become a powerful treatment alternative for many NSCLC patients, and in many cases, the first choice, giving practitioners new hope for better clinical outcomes.[61,62] Conversely, tumors possessing a reduced TMB, such as PDAC, display a scarcity of neoantigens, thereby eliciting a comparatively attenuated anti-tumor immune response.[23,63] This inherent immunogenic scarcity in PDAC is exacerbated by a notoriously dense and profoundly immunosuppressive tumor microenvironment (TME), which actively impedes effector immune cell infiltration and dampens efficient antigen presentation. Collectively, these elements result in a significantly reduced anti-tumor immune response in PDAC, significantly reducing the effectiveness of currently used immunotherapeutic techniques.[64,65]

Targeting Neoantigens: Immunotherapy in PDAC and NSCLC

The tactical targeting of neoantigens is indicative of an emergent and compelling therapeutic paradigm within the scope of NSCLC immunotherapy. Of particular interest are neoantigens originating from specific, well-defined somatic mutations within the epidermal growth factor receptor (*EGFR*) gene, such as L858R, T790M, and the E746_A750 deletion, and also *BRAF*, *MET*, *RET*, *ROS1*, *TP53*, *STK11* (*LKB1*),

PIK3CA, *NRAS*, *HRAS*, *HER2* (*ERBB2*), *MED23*, and *SNTB2*, which are distinguished by their highly tumor-restricted expression and their profound T-cell stimulatory capacity (Table 1).[66,67] Indeed, clinical studies of personalized neoantigen vaccines (PNVs) have confirmed both their positive safety record and their ability to produce significant clinical responses in groups of patients with advanced NSCLC who have these *EGFR* mutations.[67] Illustratively, in vitro models provide evidence that vaccination with peptides derived from the T790M mutation sparks a specific CTL against neoplastic cells harboring the neoantigen.[66] The therapeutic potential of such vaccines appears to be dramatically amplified through synergistic combinations with ICIs, agents like tislelizumab, or with conventional chemotherapeutic regimens. Nevertheless, the clinical translation of these strategies is hampered by challenges that are difficult to surmount, notably the intrinsic heterogeneity among *EGFR* mutant subtypes and the potential for clonal neoantigen attrition set in motion by tyrosine kinase inhibitor (TKI) therapy.[68,69] Evidence indicating that the co-occurrence of particular HLA allotypes, such as HLA-A*02:01, with *EGFR* mutations correlates with an improved prognostic outlook in affected individuals further adds another layer of complexity to this landscape while also providing opportunities for patient stratification.[70] Collectively, these observations illuminate a path towards the rational design of highly targeted, personalized combination immunotherapies for NSCLC.

Within the distinct, yet analogously challenging, context of PDAC, investigations have substantiated that even a quantitatively limited repertoire of clonal neoantigens—originating from canonical driver mutations in genes like *KRAS* (notably G12D, G12V, Q61H), *TP53* (e.g., R175H, R273H), *SMAD4*, and *CDKN2A*, supplemented by those from less frequently mutated genes including *ARID1A*, *MLL3*, *RNF43*, *TGFBR2*, and *BRCA2*—hold the potential to be efficacious targets for inducing robust T-cell-mediated anti-tumor immunity (Table 1).[23,71,72] The precise and specific identification of this neoantigenic landscape has been actualized by sophisticated technological progress in next-generation sequencing (NGS) and advanced bioinformatic algorithms, thereby critically facilitating the rational development of personalized immunotherapeutic modalities, including individualized vaccines and adoptively transferred, genetically engineered T-cells, such as T-cell receptor (TCR)-engineered T-cells and Chimeric Antigen Receptor (CAR)-T cells.[73–75] mRNA- and peptide-based neoantigen vaccines have shown a good safety profile and immunogenicity in PDAC cohorts, according to preliminary results from early-phase clinical trials. However, their monotherapeutic clinical efficacy has been limited thus far, highlighting the need for combinatorial regimens that include ICIs and TME-modulating agents.[76] Furthermore, putting into practice rapid and cost-effective methodologies for neoantigen validation, coupled with a strategic emphasis on high-fidelity clonal neoantigens, is hypothesized to mitigate the risk of immune evasion and thereby augment therapeutic efficacy.[72] At the same time, cutting-edge platform technologies, such as lipid nanoparticle (LNP)-mediated delivery vehicles and CRISPR-Cas gene-editing systems, are playing crucial roles in enhancing antigen presentation pathways and boosting the resulting adaptive immune responses. Notwithstanding the formidable challenges posed by inherent tumor heterogeneity and the intricate logistical complexities associated with personalized vaccine manufacturing, the strategic targeting of neoantigens in PDAC proffers a golden opportunity for surmounting entrenched therapeutic resistance and substantially improving patient survival outcomes. In the difficult field of treatment-refractory cancers, this therapeutic paradigm, which is distinguished by its highly selective engagement of neoplastic cells and thereby minimizes off-tumor toxicities to healthy tissues, has the profound potential to orchestrate durable anti-tumor immune responses and establish long-lived immunological memory, thereby illuminating a transformative trajectory for personalized medicine.[76]

.

Table 1. Neoantigens in NSCLC and PDAC.

Neoantigen	Properties	Applications	References
Shared Neoantigens (NSCLC & PDAC)			
KRAS (G12C, G12D, G12V, G12R, Q61H)	Driver mutation, recurrent, tumor-specific; hotspot differs per cancer type	Peptide/mRNA vaccines, TCR-T, adoptive cell therapy	77–79
TP53 mutations (R175H, R273H, others)	Tumor suppressor, immunogenic; heterogeneous; clonal in both cancers	Personalized vaccines, adoptive T-cell therapy	80, 81
Personalized frameshift/indel neoantigens	Unique per patient, predicted by sequencing	mRNA/peptide/DC vaccines	82–84
PIK3CA mutations	Driver, occasionally immunogenic	Personalized peptide vaccines	85
PTEN loss mutations	Tumor suppressor; may produce neoepitopes	Vaccine candidate in combination therapy	86
Enriched Neoantigens in NSCLC			
EGFR (L858R, T790M, E746_A750del)	Oncogenic driver; highly tumor-restricted; T-cell stimulatory; subset-specific	Peptide/mRNA vaccines, TCR-T; adjunct to EGFR inhibitors	87, 88
STK11 (*LKB1*)	Tumor suppressor; affects TME	Vaccine combination strategies; predictive biomarker	89
MET	Oncogenic driver; fusion/overexpression	Peptide/TCR vaccines	90, 91
RET	Fusion-driven oncogenic; rare but immunogenic	Personalized TCR/peptide vaccines	92–95
ROS1	Fusion-driven; highly tumor-specific	Personalized vaccine/TCR therapy	93–95
BRAF	Oncogenic driver; subset-specific	Peptide/mRNA vaccines, TCR-T	96, 97
MED23, *SNTB2*	Tumor-specific mutations	Candidate for personalized vaccines	98, 99
NRAS, *HRAS*	Rare driver mutations; immunogenic in subset	Personalized peptide/mRNA vaccines	100–103
Cancer-testis antigens (NY-ESO-1, MAGE-A, XAGE1)	Tumor-restricted expression; immunogenic	Peptide/protein vaccines, TCR/CAR-T	85, 104–106

Published by Tehran University of Medical Sciences (http://ijaai.tums.ac.ir)

Table 1. Continued...

Neoantigen	Properties	Applications	References
Enriched Neoantigens in PDAC			
SMAD4	Tumor suppressor loss; patient-specific	Personalized neoantigen vaccines	78, 107, 108
CDKN2A	Tumor suppressor loss; heterogeneous	Personalized peptide/mRNA vaccines	78, 107
BRCA1/2 & DNA repair defects	Increase indels → neoantigen load; subset-specific	Neoantigen vaccines + PARP inhibitors or checkpoint blockade	109–111
ARID1A	Less frequent mutation; clonal	Personalized vaccine candidates	82
MLL3 (*KMT2C*)	Chromatin modifier; neoepitopes in subsets	Candidate for mRNA/DC vaccines	82
RNF43	Frameshift mutation; immunogenic	Personalized vaccine candidates	82
TGFBR2	Frameshift mutation; immunogenic	Peptide/mRNA vaccine	82
Mesothelin, MUC1, CEACAM5	Overexpressed tumor antigens, sometimes neo-epitopic	Protein/peptide vaccines, CAR-T/NK, ADCs	112, 113

ADC: antibody-drug conjugate; ARID1A: AT-rich interaction domain 1A; BRAF: B-Raf proto-oncogene, serine/threonine kinase; BRCA: breast cancer gene; CAR-T: chimeric antigen receptor T-cell; CD: cluster of differentiation; CDKN2A: cyclin dependent kinase inhibitor 2A; CEACAM5: carcinoembryonic antigen related cell adhesion molecule 5; DC: dendritic cell; del: deletion; DNA: deoxyribonucleic acid; EGFR: epidermal growth factor receptor; HRAS: HRas proto-oncogene, GTPase; KMT2C: lysine methyltransferase 2C; KRAS: KRAS proto-oncogene, GTPase; LKB1: liver kinase B1; MED23: mediator complex subunit 23; MET: MET proto-oncogene, receptor tyrosine kinase; MLL3: mixed-lineage leukemia 3; MUC1: mucin 1, cell surface associated; NK: natural killer; NRAS: NRAS proto-oncogene, GTPase; NSCLC: non-small cell lung cancer; NY-ESO-1: New York esophageal squamous cell carcinoma 1; PARP: poly(ADP-ribose) polymerase; PDAC: pancreatic ductal adenocarcinoma; PIK3CA: phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; PTEN: phosphatase and tensin homolog; RET: ret proto-oncogene; RNF43: ring finger protein 43; ROS1: ROS proto-oncogene 1, receptor tyrosine kinase; SMAD4: SMAD family member 4; SNTB2: syntrophin beta 2; STK11: serine/threonine kinase 11; TCR-T: T-cell receptor-engineered T-cell; TGFBR2: transforming growth factor beta receptor 2; TME: tumor microenvironment; TP53: tumor protein p53; XAGE1: X antigen family member 1.

Conclusion and Future Perspectives

This review clearly illustrates that the quantitative and qualitative disparities in neoantigen profiles between NSCLC and PDAC play a crucial role in shaping their differential responses to immunotherapy. The substantial mutational burden and pronounced neoantigenic diversity characteristic of NSCLC support the more potent efficacy of immune-based interventions in this malignancy versus PDAC. Furthermore, a body of literature gives weight to the assertion that the immunogenic quality of NSCLC-derived neoantigens, having their roots in somatic mutations and gene fusions yielding high-affinity binding MHC molecules, results in a more potent stimulation of anti-tumor immune responsesIn fact, new data show that neoantigen quality frequently surpasses quantity, which is a crucial factor in the better immunotherapeutic results seen in NSCLC patients as opposed to those with PDAC (Figure.1). Regular studies show that neoantigens derived from NSCLC are generally very immunogenic and can elicit strong and specific T-cell-mediated effector functions. This has been confirmed in a variety of experimental settings, including in vitro tests and in vivo animal models.

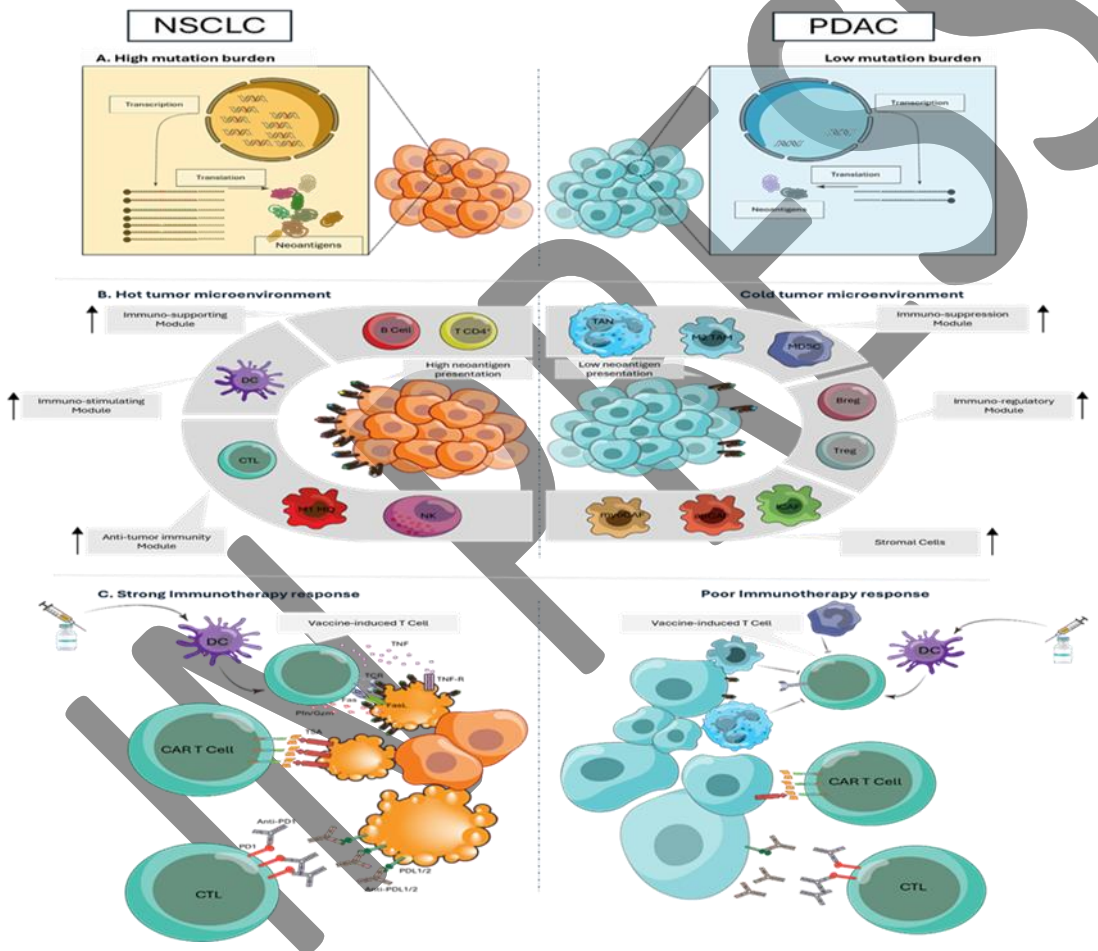

Figure 1:Comparison of molecular and cellular mechanisms affecting immunotherapy response in NSCLC and PDAC. (A) NSCLC shows high mutation burden and increased neoantigen production; PDAC has low mutation burden and fewer neoantigens. (B) NSCLC tumors present more neoantigens and attract active immune cells ("hot" TME); PDAC shows limited presentation and immunosuppressive infiltration ("cold" TME). (C) These differences result in stronger immunotherapy response in NSCLC and poor response in PDAC. NSCLC: Non-Small Cell Lung Cancer, PDAC: Pancreatic Ductal Adenocarcinoma, DC: Dendritic Cell, CTL: Cytotoxic T Lymphocyte, TAN: Tumor-Associated Neutrophil, MDSC: Myeloid-Derived Suppressor Cell, Breg: Regulatory B Cell, Treg: Regulatory T Cell, NK: Natural Killer Cell, MQ: Macrophage, iCAF: Inflammatory Cancer-Associated Fibroblast, myCAF; Myofibroblastic CAF, apCAF: Antigen-Presenting CAF, CAR-T: Chimeric Antigen Receptor T Cell, PD1/PD-L1: Programmed Death 1/Ligand 1.

Published by Tehran University of Medical Sciences (http://ijaai.tums.ac.ir)

On the other hand, PDAC manifests a marked and well-established resistance to standard immunotherapeutic approaches, which is exacerbated by the marked deficiency and poor immunogenic quality of its neoantigens as well as an intrinsically immunosuppressive TME. The development of progressively individualized therapeutic interventions has been facilitated by the accurate identification and careful characterization of genuine clonal and subclonal neoantigens driven by significant technological advancements in NGS and advanced bioinformatic algorithms. Additionally, there is significant room for growth in boosting treatment effectiveness in immunotherapeutically resistant cancers like PDAC by carefully combining neoantigen-directed approaches-like customized vaccines or adoptive T-cell therapies-with therapies that target the hostile TME and with well-established immune checkpoint inhibitors.

This quickly developing field is well-positioned to benefit from novel multivalent vaccine formulations and flexible mRNA platforms in the future, thanks to the synergistic integration of cutting-edge genomics, proteomics, and artificial intelligence technologies. These next-generation strategies are being developed to simultaneously target a wide range of patient-specific neoantigens in an effort to overcome the significant obstacles presented by intra- and inter-tumor heterogeneity. In conclusion, all of the evidence points to the urgent need for innovative approaches to neoantigen targeting and calls for more thorough research to overcome the intricate treatment challenges that resistant cancers present. A paradigm where neoantigens play multifaceted roles that go beyond direct therapeutics to include the sensitive monitoring of treatment response, the early detection of incipient relapse, and possibly the accurate prediction of emergent therapeutic resistance in individual patients is envisioned by this perspective, which lays out new and promising avenues for the development of personalized immunotherapy.

STATEMENT OF ETHICS

Not applicable.

FUNDING

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ACKNOWLEDGMENTS

Not applicable.

DATA AVAILABILITY

Not applicable.

AI ASSISTANCE DISCLOSURE

Not applicable.

REFERENCES

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024 May-Jun;74(3):229-263. doi: 10.3322/caac.21834. Epub 2024 Apr 4. PMID: 38572751.
2. Eskandari-Malayeri F, Rezaei M. Immune checkpoint inhibitors as mediators for immunosuppression by cancer-associated fibroblasts: a comprehensive review. Front Immunol. 2022;13:996145.
3. Siegel RL, Kratzer TB, Giaquinto AN, Sung H, Jemal A. Cancer statistics, 2025. CA Cancer J Clin. 2025;75(1):10-45.
4. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209-49.
5. Kumar M, Sarkar A. Current therapeutic strategies and challenges in NSCLC treatment: a comprehensive review. Exp Oncol. 2022;44(1):7-16.
6. Orth M, Metzger P, Gerum S, Mayerle J, Schneider G, Belka C, et al. Pancreatic ductal adenocarcinoma: biological hallmarks, current status, and future perspectives of combined modality treatment approaches. Radiat Oncol. 2019;14(1):141.
7. Shekarchian S, Eghtedardoost M, Golshahi H, Behrouzfar H, Fakhroueian Z, Yaraee R. A Novel Nanodrug Suppresses Lung Cancer Growth and Metastasis in C57BL/6 Mouse Model by Altering CD8+ Cell Infiltration

and Oxidative Stress. Iran J Allergy Asthma Immunol. 2025:1-21.
8. Gupta SL, Basu S, Soni V, Jaiswal RK. Immunotherapy: an alternative promising therapeutic approach against cancers. Mol Biol Rep. 2022;49(10):9903-9913.
9. Subramaniam DS, Liu SV, Giaccone G. Novel approaches in cancer immunotherapy. Discov Med. 2016;21(116):267-74.
10. Szeto GL, Finley SD. Integrative Approaches to Cancer Immunotherapy. Trends Cancer. 2019;5(7):400-410.
11. Hendriks LEL, Remon J, Faivre-Finn C, Garassino MC, Heymach JV, Kerr KM, et al. Non-small-cell lung cancer. Nat Rev Dis Primers. 2024;10(1):71.
12. Non-Small Cell Lung Cancer Treatment (PDQ®)–Patient Version. May 23, 2025. Accessed [Date of access]. https://www.cancer.gov/types/lung/patient/non-small-cell-lung-treatment-pdq#:~:text=Key%20Points, to%20 get%20a%20second%20opinion.
13. Heineman DJ, Daniels JM, Schreurs WH. Clinical staging of NSCLC: current evidence and implications for adjuvant chemotherapy. Ther Adv Med Oncol. 2017;9(9):599-609.
14. Alduais Y, Zhang H, Fan F, Chen J, Chen B. Non-small cell lung cancer (NSCLC): A review of risk factors, diagnosis, and treatment. Medicine (Baltimore). 2023;102(8):e32899.
15. Kaur P, Singh SK, Mishra MK, Singh S, Singh R. Promising Combinatorial Therapeutic Strategies against Non-Small Cell Lung Cancer. Cancers (Basel). 2024;16(12).
16. Sham NO, Zhao L, Zhu Z, Roy TM, Xiao H, Bai Q, et al. Immunotherapy for Non-small Cell Lung Cancer: Current Agents and Potential Molecular Targets. Anticancer Res. 2022;42(7):3275-84.
17. Yoh K, Matsumoto S, Furuya N, Nishino K, Miyamoto S, Oizumi S, et al. Comprehensive assessment of PD-L1 expression, tumor mutational burden and oncogenic driver alterations in non-small cell lung cancer patients treated with immune checkpoint inhibitors. Lung Cancer. 2021;159:128-34.
18. Olivares-Hernández A, González Del Portillo E, Tamayo-Velasco Á, Figuero-Pérez L, Zhilina-Zhilina S, Fonseca-Sánchez E, et al. Immune checkpoint inhibitors in non-small cell lung cancer: from current perspectives to future treatments-a systematic review. Ann Transl Med. 2023;11(10):354.
19. Kang J, Zhang C, Zhong WZ. Neoadjuvant immunotherapy for non-small cell lung cancer: State of the art. Cancer Commun (Lond). 2021;41(4):287-302.
20. Shukla N, Hanna N. Neoadjuvant and Adjuvant Immunotherapy in Early-Stage Non-Small Cell Lung Cancer. Lung Cancer (Auckl). 2021;12:51-60.
21. Hansen T, Hill J, Tincknell G, Siu D, Brungs D, Clingan P, et al. Evidence for the evolving role of neoadjuvant and perioperative immunotherapy in resectable non-small cell lung cancer. Explor Target Antitumor Ther. 2024;5(6):1247-60.
22. Ying H, Kimmelman AC, Bardeesy N, Kalluri R, Maitra A, DePinho RA. Genetics and biology of pancreatic ductal adenocarcinoma. Genes Dev. 2025;39(1-2):36-63.
23. Singh G, Kutcher D, Lally R, Rai V. Targeting Neoantigens in Pancreatic Ductal Adenocarcinoma. Cancers (Basel). 2024;16(11).
24. Joseph AM, Al Aiyan A, Al-Ramadi B, Singh SK, Kishore U. Innate and adaptive immune-directed tumour microenvironment in pancreatic ductal adenocarcinoma. Front Immunol. 2024;15:1323198.
25. Olaoba OT, Yang M, Adelusi TI, Maidens T, Kimchi ET, Staveley-O'Carroll KF, Li G. Targeted Therapy for Highly Desmoplastic and Immunosuppressive Tumor Microenvironment of Pancreatic Ductal Adenocarcinoma. Cancers (Basel). 2024;16(8).
26. Alzhrani R, Alsaab HO, Vanamal K, Bhise K, Tatiparti K, Barari A, et al. Overcoming the Tumor Microenvironmental Barriers of Pancreatic Ductal Adenocarcinomas for Achieving Better Treatment Outcomes. Adv Ther (Weinh). 2021;4(6).
27. Pang Y, Holmes MV, Chen Z, Kartsonaki C. A review of lifestyle, metabolic risk factors, and blood-based biomarkers for early diagnosis of pancreatic ductal adenocarcinoma. J Gastroenterol Hepatol. 2019;34(2):330-45.
28. Gardiner A, Kidd J, Elias MC, Young K, Mabey B, Taherian N, et al. Pancreatic Ductal Carcinoma Risk Associated With Hereditary Cancer-Risk Genes. J Natl Cancer Inst. 2022;114(7):996-1002.
29. McGarry JL, Creavin B, Kelly ME, Gallagher TK. Risk of pancreatic ductal adenocarcinoma associated with carriage of BRCA1 and/or BRCA2 mutation: A systematic review and meta-analysis. J Surg Oncol. 2022;126(6):1028-37.
30. Keane MG, Horsfall L, Rait G, Pereira SP. A case-control study comparing the incidence of early symptoms in pancreatic and biliary tract cancer. BMJ Open. 2014;4(11):e005720.
31. Gullo L, Tomassetti P, Migliori M, Casadei R, Marrano D. Do early symptoms of pancreatic cancer exist that can allow an earlier diagnosis? Pancreas. 2001;22(2):210-3.

32. Kunovsky L, Tesarikova P, Kala Z, Kroupa R, Kysela P, Dolina J, Trna J. The Use of Biomarkers in Early Diagnostics of Pancreatic Cancer. Can J Gastroenterol Hepatol. 2018;2018:5389820.
33. Mangge H, Niedrist T, Renner W, Lyer S, Alexiou C, Haybaeck J. New Diagnostic and Therapeutic Aspects of Pancreatic Ductal Adenocarcinoma. Curr Med Chem. 2017;24(28):3012-24.
34. Sarantis P, Koustas E, Papadimitropoulou A, Papavassiliou AG, Karamouzis MV. Pancreatic ductal adenocarcinoma: Treatment hurdles, tumor microenvironment and immunotherapy. World J Gastrointest Oncol. 2020;12(2):173-81.
35. Poyia F, Neophytou CM, Christodoulou MI, Papageorgis P. The Role of Tumor Microenvironment in Pancreatic Cancer Immunotherapy: Current Status and Future Perspectives. Int J Mol Sci. 2024;25(17).
36. Macherla S, Laks S, Naqash AR, Bulumulle A, Zervos E, Muzaffar M. Emerging Role of Immune Checkpoint Blockade in Pancreatic Cancer. Int J Mol Sci. 2018;19(11).
37. Kabacaoglu D, Ciecielski KJ, Ruess DA, Algül H. Immune Checkpoint Inhibition for Pancreatic Ductal Adenocarcinoma: Current Limitations and Future Options. Front Immunol. 2018;9:1878.
38. Levink IJM, Brosens LAA, Rensen SS, Aberle MR, Olde Damink SSW, Cahen DL, et al. Neoantigen Quantity and Quality in Relation to Pancreatic Cancer Survival. Front Med (Lausanne). 2021;8:751110.
39. Liang H, Xu Y, Chen M, Zhao J, Zhong W, Liu X, et al. Characterization of Somatic Mutations That Affect Neoantigens in Non-Small Cell Lung Cancer. Front Immunol. 2021;12:749461.
40. McGranahan N, Furness AJ, Rosenthal R, Ramskov S, Lyngaa R, Saini SK, et al. Clonal neoantigens elicit T cell immunoreactivity and sensitivity to immune checkpoint blockade. Science. 2016;351(6280):1463-9.
41. Su S, Chen F, Xu M, Liu B, Wang L. Recent advances in neoantigen vaccines for treating non-small cell lung cancer. Thorac Cancer. 2023;14(34):3361-8.
42. De Mattos-Arruda L, Vazquez M, Finotello F, Lepore R, Porta E, Hundal J, et al. Neoantigen prediction and computational perspectives towards clinical benefit: recommendations from the ESMO Precision Medicine Working Group. Ann Oncol. 2020;31(8):978-90.
43. Sasada T. [Cancer immunotherapy targeting neoantigens derived from tumor-specific gene mutations]. Nihon Rinsho. 2017;75(2):189-95.
44. Mardis ER. Neoantigens and genome instability: impact on immunogenomic phenotypes and immunotherapy response. Genome Med. 2019;11(1):71.
45. Levine AJ, Jenkins NA, Copeland NG. The Roles of Initiating Truncal Mutations in Human Cancers: The Order of Mutations and Tumor Cell Type Matters. Cancer Cell. 2019;35(1):10-15.
46. Habel K. Resistance of Polyoma Virus Immune Animals to Transplanted Polyoma Tumors. Proc Soc Exp Biol Med. 1961;106:722-5.
47. Sim MJW, Sun PD. T Cell Recognition of Tumor Neoantigens and Insights Into T Cell Immunotherapy. Front Immunol. 2022;13:833017.
48. Bobisse S, Foukas PG, Coukos G, Harari A. Neoantigen-based cancer immunotherapy. Ann Transl Med. 2016;4(14):262.
49. Schumacher TN, Schreiber RD. Neoantigens in cancer immunotherapy. Science. 2015;348(6230):69-74.
50. Ohue Y. [Current Topics of Cancer Antigen]. Gan To Kagaku Ryoho. 2019;46(10):1467-72.
51. Xie N, Shen G, Gao W, Huang Z, Huang C, Fu L. Neoantigens: promising targets for cancer therapy. Signal Transduct Target Ther. 2023;8(1):9.
52. Jiang T, Shi T, Zhang H, Hu J, Song Y, Wei J, et al. Tumor neoantigens: from basic research to clinical applications. J Hematol Oncol. 2019;12(1):93.
53. Wu DW, Jia SP, Xing SJ, Ma HL, Wang X, Tang QY, et al. Personalized neoantigen cancer vaccines: current progression, challenges and a bright future. Clin Exp Med. 2024;24(1):229.
54. Ward JP, Gubin MM, Schreiber RD. The Role of Neoantigens in Naturally Occurring and Therapeutically Induced Immune Responses to Cancer. Adv Immunol. 2016;130:25-74.
55. Wang P, Chen Y, Wang C. Beyond Tumor Mutation Burden: Tumor Neoantigen Burden as a Biomarker for Immunotherapy and Other Types of Therapy. Front Oncol. 2021;11:672677.
56. Zou XL, Li XB, Ke H, Zhang GY, Tang Q, Yuan J, et al. Prognostic Value of Neoantigen Load in Immune Checkpoint Inhibitor Therapy for Cancer. Front Immunol. 2021;12:689076.
57. Lang F, Schrörs B, Löwer M, Türeci Ö, Sahin U. Identification of neoantigens for individualized therapeutic cancer vaccines. Nat Rev Drug Discov. 2022;21(4):261-82.
58. Pao SC, Chu MT, Hung SI. Therapeutic Vaccines Targeting Neoantigens to Induce T-Cell Immunity against Cancers. Pharmaceutics. 2022;14(4).

59. Liontos M, Anastasiou I, Bamias A, Dimopoulos MA. DNA damage, tumor mutational load and their impact on immune responses against cancer. Ann Transl Med. 2016;4(14):264.
60. Goodman AM, Kato S, Bazhenova L, Patel SP, Frampton GM, Miller V, et al. Tumor Mutational Burden as an Independent Predictor of Response to Immunotherapy in Diverse Cancers. Mol Cancer Ther. 2017;16(11):2598-608.
61. Rizvi NA, Hellmann MD, Snyder A, Kvistborg P, Makarov V, Havel JJ, et al. Cancer immunology. Mutational landscape determines sensitivity to PD-1 blockade in non-small cell lung cancer. Science. 2015;348(6230):124-8.
62. Xiong A, Wang J, Zhou C. Immunotherapy in the First-Line Treatment of NSCLC: Current Status and Future Directions in China. Front Oncol. 2021;11:757993.
63. Bear AS, Vonderheide RH, O'Hara MH. Challenges and Opportunities for Pancreatic Cancer Immunotherapy. Cancer Cell. 2020;38(6):788-802.
64. Li KY, Yuan JL, Trafton D, Wang JX, Niu N, Yuan CH, et al. Pancreatic ductal adenocarcinoma immune microenvironment and immunotherapy prospects. Chronic Dis Transl Med. 2020;6(1):6-17.
65. Looi CK, Chung FF, Leong CO, Wong SF, Rosli R, Mai CW. Therapeutic challenges and current immunomodulatory strategies in targeting the immunosuppressive pancreatic tumor microenvironment. J Exp Clin Cancer Res. 2019;38(1):162.
66. Li F, Wu H, Du X, Sun Y, Rausseo BN, Talukder A, et al. Epidermal Growth Factor Receptor-Targeted Neoantigen Peptide Vaccination for the Treatment of Non-Small Cell Lung Cancer and Glioblastoma. Vaccines (Basel). 2023;11(9):1460.
67. Li F, Deng L, Jackson KR, Talukder AH, Katailiha AS, Bradley SD, et al. Neoantigen vaccination induces clinical and immunologic responses in non-small cell lung cancer patients harboring EGFR mutations. J Immunother Cancer. 2021;9(7):e002531.
68. Shi C, Wang Y, Xue J, Zhou X. Immunotherapy for EGFR-mutant advanced non-small-cell lung cancer: Current status, possible mechanisms and application prospects. Front Immunol. 2022;13:940288.
69. Al Bakir M, Reading JL, Gamble S, Rosenthal R, Uddin I, Rowan A, et al. Clonal driver neoantigen loss under EGFR TKI and immune selection pressures. Nature. 2025;639(8056):1052-59.
70. Dimou A, Grewe P, Sidney J, Sette A, Norman PJ, Doebele RC. HLA Class I Binding of Mutant EGFR Peptides in NSCLC Is Associated With Improved Survival. J Thorac Oncol. 2021 Jan;16(1):104-112. doi: 10.1016/j.jtho.2020.08.023. Epub 2020 Sep 11. PMID: 32927123; PMCID: PMC7797166.
71. Issue Information. Immunol Rev. 2023;310(1):1-3.
72. Balachandran VP, Łuksza M, Zhao JN, Makarov V, Moral JA, Remark R, et al. Identification of unique neoantigen qualities in long-term survivors of pancreatic cancer. Nature. 2017;551(7681):512-6.
73. Hu Z, Ott PA, Wu CJ. Towards personalized, tumour-specific, therapeutic vaccines for cancer. Nat Rev Immunol. 2018;18(3):168-82.
74. Blass E, Ott PA. Advances in the development of personalized neoantigen-based therapeutic cancer vaccines. Nat Rev Clin Oncol. 2021;18(4):215-29.
75. Kumari K, Singh A, Chaudhary A, Singh RK, Shanker A, Kumar V, Haque R. Neoantigen Identification and Dendritic Cell-Based Vaccines for Lung Cancer Immunotherapy. Vaccines (Basel). 2024;12(5).
76. Singh G, Kutcher D, Lally R, Rai V. Targeting Neoantigens in Pancreatic Ductal Adenocarcinoma. Cancers (Basel). 2024;16(11):2101.
77. Pant S, Wainberg ZA, Weekes CD, Furqan M, Kasi PM, Devoe CE, et al. Lymph-node-targeted, mKRAS-specific amphiphile vaccine in pancreatic and colorectal cancer: the phase 1 AMPLIFY-201 trial. Nat Med. 2024;30(2):531-42.
78. Stefanoudakis D, Frountzas M, Schizas D, Michalopoulos NV, Drakaki A, Toutouzas KG. Significance of TP53, CDKN2A, SMAD4 and KRAS in Pancreatic Cancer. Curr Issues Mol Biol. 2024;46(4):2827-44.
79. Lennerz V, Doppler C, Fatho M, Dröge A, Schaper S, Gennermann K, et al. T-cell receptors identified by a personalized antigen-agnostic screening approach target shared neoantigen KRAS Q61H. Front Immunol. 2025;16:1509855.
80. Steinbuck MP, Cabana-Puig X, Palmer E, Jung MM, Williams T, Osaer K, et al. AMP-peptide vaccination against multiple p53 mutant epitopes promotes lymph node delivery to generate potent, functional T cell immunity. Cancer Res. 2024;84(6_Supplement):4099.
81. Duffy MJ, Synnott NC, Crown J. Mutant p53 as a target for cancer treatment. Eur J Cancer. 2017;83:258-265.
82. Rojas LA, Sethna Z, Soares KC, Olcese C, Pang N, Patterson E, et al. Personalized RNA neoantigen vaccines stimulate T cells in pancreatic cancer. Nature. 2023;618(7963):144-50.
83. Ding Z, Li Q, Zhang R, Xie L, Shu Y, Gao S, et al. Personalized neoantigen pulsed dendritic cell vaccine for advanced lung cancer. Signal Transduct Target Ther. 2021;6(1):26.

84. Ott PA, Hu Z, Keskin DB, Shukla SA, Sun J, Bozym DJ, et al. An immunogenic personal neoantigen vaccine for patients with melanoma. Nature. 2017;547(7662):217-21.
85. Magoola M, Niazi SK. Current Progress and Future Perspectives of RNA-Based Cancer Vaccines: A 2025 Update. Cancers (Basel). 2025;17(11):1882.
86. Singh P, Khatib MN, R R, Kaur M, Srivastava M, Barwal A, et al. Advancements and challenges in personalized neoantigen-based cancer vaccines. Oncol Rev. 2024;19:1541326.
87. Li F, Deng L, Jackson KR, Talukder AH, Katailiha AS, Bradley SD, et al. Neoantigen vaccination induces clinical and immunologic responses in non-small cell lung cancer patients harboring EGFR mutations. J Immunother Cancer. 2021;9(7).
88. Yang H, Wang Y, Jia Z, Wang Y, Yang X, Wu P, et al. Characteristics of T-Cell Receptor Repertoire and Correlation With EGFR Mutations in All Stages of Lung Cancer. Front Oncol. 2021;11:537735.
89. Skoulidis F, Goldberg ME, Greenawalt DM, Hellmann MD, Awad MM, Gainor JF, et al. STK11/LKB1 Mutations and PD-1 Inhibitor Resistance in KRAS-Mutant Lung Adenocarcinoma. Cancer Discov. 2018;8(7):822-35.
90. Minne RL, Luo NY, Traynor AM, Huang M, DeTullio L, Godden J, et al. Genomic and Immune Landscape Comparison of MET Exon 14 Skipping and MET-Amplified Non-small Cell Lung Cancer. Clin Lung Cancer. 2024;25(6):567-576.e1.
91. Su S, Luo P, Zhang J, Zhang B, Zou J, Huang Z. P14. 12 MET amplification and immune checkpoint inhibitor efficacy in NSCLC. J Thorac Oncol. 2021;16(3):S334.
92. Lu C, Dong XR, Zhao J, Zhang XC, Chen HJ, Zhou Q, et al. Association of genetic and immuno-characteristics with clinical outcomes in patients with RET-rearranged non-small cell lung cancer: a retrospective multicenter study. J Hematol Oncol. 2020;13(1):37.
93. Jiang B, Hu L, Dong D, Guo Z, Wei W, Wang C, et al. TP53 or CDKN2A/B covariation in ALK/RET/ROS1-rearranged NSCLC is associated with a high TMB, tumor immunosuppressive microenvironment and poor prognosis. J Cancer Res Clin Oncol. 2023;149(12):10041-52.
94. Ingels J, De Cock L, Stevens D, Mayer RL, Thery F, Sanchez GS, et al. Neoantigen-targeted dendritic cell vaccination in lung cancer patients induces long-lived T cells exhibiting the full differentiation spectrum. Cell Rep Med. 2024;5(5).
95. Robertson J, Salm M, Dangl M. Adoptive cell therapy with tumour-infiltrating lymphocytes: the emerging importance of clonal neoantigen targets for next-generation products in non-small cell lung cancer. Immuno-Oncology Technology. 2019;3:1-7.
96. Case K, Kennedy K, Kujtan L, Subramanian J. The role of tumour neoantigens in the differential response to immunotherapy (IO) in EGFR and BRAF mutated lung cancers: Quantity or quality? Ann Oncol. 2019;30:v513.
97. Lin J, Liu J, Hao SG, Lan B, Zheng XB, Xiong JN, et al. An EGFR L858R mutation identified in 1862 Chinese NSCLC patients can be a promising neoantigen vaccine therapeutic strategy. Front Immunol. 2022;13:1022598.
98. Hachey SJ, Forsythe AG, Keshava HB, Hughes CCW. ImmuniT Platform for Improved Neoantigen Prediction in Lung Cancer. bioRxiv. 2025.
99. Fu X, Liu S, Cao D, Li C, Ji H, Wang G. Med23 deficiency reprograms the tumor microenvironment to promote lung tumorigenesis. Br J Cancer. 2024;130(5):716-27.
100. Yan Y, Gao Z, Han H, Zhao Y, Zhang Y, Ma X, Chen H. NRAS expression is associated with prognosis and tumor immune microenvironment in lung adenocarcinoma. J Cancer Res Clin Oncol. 2022;148(3):565-75.
101. Chen GL, Kong DX, Lin Y. Neo-Antigen-Reactive T Cells Immunotherapy for Colorectal Cancer: A More Personalized Cancer Therapy Approach. Global Challenges. 2023;7(11):2200186.
102. Hattori T, Maso L, Araki KY, Koide A, Hayman J, Akkapeddi P, et al. Creating MHC-restricted neoantigens with covalent inhibitors that can be targeted by immune therapy. Cancer Discov. 2023;13(1):132-45.
103. Dehem A, Mazieres J, Chour A, Guisier F, Ferreira M, Boussageon M, et al. Characterization of 164 patients with NRAS mutated non-small cell lung cancer (NSCLC). Lung Cancer. 2023;186:107393.
104. Yang P, Qiao Y, Meng M, Zhou Q. Cancer/Testis Antigens as Biomarker and Target for the Diagnosis, Prognosis, and Therapy of Lung Cancer. Front Oncol. 2022;12:864159.
105. Saito K, Nakayama E, Valmori D. Immune Responses to the Cancer Testis Antigen XAGE-1b in Non Small Cell Lung Cancer Caucasian Patients. PLoS One. 2016;11(3):e0150623.
106. Scanlan MJ, Gure AO, Jungbluth AA, Old LJ, Chen YT. Cancer/testis antigens: an expanding family of targets for cancer immunotherapy. Immunol Rev. 2002;188:22-32.
107. Connor AA, Denroche RE, Jang GH, Timms L, Kalimuthu SN, Selander I, et al. Association of Distinct Mutational Signatures With Correlates of Increased Immune Activity in Pancreatic Ductal Adenocarcinoma. JAMA Oncol. 2017;3(6):774-83.

108. Chen YW, Hsiao PJ, Weng CC, Kuo KK, Kuo TL, Wu DC, et al. SMAD4 Loss triggers the phenotypic changes of pancreatic ductal adenocarcinoma cells. BMC Cancer. 2014;14:1.
109. Domchek SM, McWilliams R, Hendifar A, Shroff RT, Leichman L, Epelbaum R, et al. Abstract B102: A phase 2, open-label study of the PARP inhibitor rucaparib in patients with pancreatic cancer and a known deleterious BRCA mutation. Cancer Res. 2015;75(13_Supplement):B102-B.
110. Seeber A, Zimmer K, Kocher F, Puccini A, Xiu J, Nabhan C, et al. Molecular characteristics of BRCA1/2 and PALB2 mutations in pancreatic ductal adenocarcinoma. ESMO Open. 2020;5(6):e000942.
111. Lei M, Gai J, McPhaul TJ, Luo H, Lin P, Liu D, et al. Homologous recombination-DNA damage response defects increase TMB and neoantigen load, but not effector T cell density and clonal diversity in pancreatic cancer. Exp Hematol Oncol. 2025;14(1):86.
112. DeSelm CJ, Tano ZE, Varghese AM, Adusumilli PS. CAR T-cell therapy for pancreatic cancer. J Surg Oncol. 2017;116(1):63-74.
113. Giurini EF, Ralph O, Pappas SG, Gupta KH. Looking Beyond Checkpoint Inhibitor Monotherapy: Uncovering New Frontiers for Pancreatic Cancer Immunotherapy. Mol Cancer Ther. 2025;24(1):18-32.