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ORIGINAL RESEARCH ARTICLE

A novel ultraviolet-associated gene signature to predict prognosis and immunological features in patients with skin melanoma

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Abstract

Introduction: Research on the impact of ultraviolet (UV)-related genes on the prognosis of melanoma is rare.

Objective: This study aimed to explore the role of UV-associated genes in skin melanoma and their impact on prognosis.

Methods: We evaluated the prognostic implications of UV-associated genes in cutaneous melanoma and developed a predictive model for patient outcomes utilizing skin melanoma datasets sourced from The Cancer Genome Atlas. Subsequently, we investigated the correlation between UV-associated genes and the local immune environment within cutaneous melanoma.

Results: The developed prognostic model for cutaneous melanoma holds significant value for clinicians in assessing patient outcomes. The expression levels of UV-associated genes appear to influence the infiltration degree of various immune cells within the tumor microenvironment, including T cells and M1 macrophages. In addition, the model was able to predict melanoma prognosis and stratify melanoma patients, with patients in the high-risk group having a worse prognosis. Results also indicated that the high-risk group exhibited reduced infiltration of cytotoxic immune cells in the tumor tissue than the low-risk group.

Conclusion: The findings from this novel study have the potential to identify new therapeutic targets in treating cutaneous melanoma.

Keywords: Ultraviolet-associated genes; Skin melanoma; Prognosis; Immune infiltration; Drug prediction

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1. Introduction

The skin is the largest organ of the human body. Alarmingly, one person dies from skin cancer every 4 min. In 2018, the International Agency for Research on Cancer[1] projected that there would be approximately 1.52 million new skin cancer cases and 121,000 related deaths for the year 2020. Skin cancer is the most predominant form of cancer globally, accounting for 75% of all cancer cases,[2] with melanoma representing the most prevalent form of skin cancer. According to projections by the International Agency for Research on Cancer, over the next two decades, the incidence and mortality rates of melanoma are expected to rise by 78% and 73%, respectively. Melanoma is the most lethal form of skin cancer, arising from the malignant

transformation of melanocytes. Melanocytes originate from the neuroectoderm and then migrate extensively throughout the body, including the skin, uvea, mucosa, inner ear, and rectum. They are highly dendritic cells, producing melanin to resist light damage. Due to the widespread distribution of melanocytes, melanoma can develop virtually anywhere in the body, regardless of the anatomical location or the type of organs and tissues.[3] The incidence rate and mortality of melanoma vary across countries. Its prevalence is notably elevated in regions such as Australia, New Zealand, Europe, and North America, while it is lowest in Africa. This disparity is attributed to ethnicity, lifestyle choices, and genetic predispositions.[4] The distribution of melanoma subtypes and their pathogenic mechanisms vary across different populations. Individuals of Caucasian descent with fair skin predominantly develop cutaneous melanoma, primarily attributed to ultraviolet (UV) radiation exposure. In contrast, a significant proportion of individuals from Asian and African ethnicities with darker skin tones are more prone to acral and mucosal melanoma, although with a relatively lower incidence rate. Acral melanoma often develops in areas that have experienced previous injury, infection, or persistent ulceration.[5] In 2021, there were 106,110 new cases of melanoma in the United States, and 7,180 individuals succumbed to the disease.[6] In the past decades, the mortality of melanoma patients has significantly decreased due to the revolutionary progress of early diagnosis, accurate screening methods, and improved surgical principles. However, despite the reduction, the mortality rate has not improved, with a 5-year survival rate of about 27%.[6]

Risk factors for melanoma, substantiated by robust epidemiological evidence, encompass UV radiation, the presence of numerous moles, a positive family history of melanoma, and fair skin complexion. Epidemiological studies conducted through systematic reviews and meta-analyses show that individuals under 35 exposed to intense intermittent UV radiation[7] through sunbathing or indoor tanning, even in childhood, have the highest risk of developing melanoma. Intense UV radiation can induce genetic changes, such as DNA damage[8] and genetic mutations.[9] The accumulation of reactive oxygen species (ROS) and subsequent oxidative stress, along with inflammatory responses characterized by macrophage and neutrophil infiltration, are closely associated with the malignant transformation of melanocytes.[10,11] It should be noted that UV radiation is one of the two etiological mechanisms of melanoma. Early and frequent sun exposure, along with a predisposition to developing nevi, often contributes to the development of melanoma driven by *BRAF* mutations. Individuals with these risk factors are typically diagnosed at a younger age and usually present with superficial spreading melanoma, particularly on the trunk. In contrast, prolonged sun exposure is more commonly associated with *NRAS*-mutated melanoma, which typically occurs without a nevus-forming tendency.[12] In addition to environmental UV rays and certain phenotypic characteristics of individuals related to the development of skin melanoma, other factors have been proven to be related to non-skin melanoma. Some reports also indicate that acral melanoma may occur after trauma or infection, and chronic ulcer lesions.[13-15] The tumor-promoting effects of trauma and chronic inflammation may stem from elevated levels of cytokines and ROS, which can trigger genetic instability in melanocytes or activate oncogenic pathways.[10]

Over the last few decades, significant advancements in understanding melanoma pathogenesis, groundbreaking developments in targeted therapies for driver gene mutations, and immune checkpoint modulation have dramatically transformed melanoma treatment. Before 2010, therapeutic options for metastatic melanoma were limited to dacarbazine-based chemotherapy and high-dose interleukin (IL) 2, which were the only U.S Food and Drug Administration-approved treatments at the time. Interferon alpha 2b is also used as an adjuvant.[16,17] Now, many therapeutic agents and combination methods have been approved by the U.S Food and Drug Administration, including immunotherapy,[18,19] targeted therapy,[3] and oncolytic herpesvirus talimogene laherparepvec.[20,21] These therapeutic approaches have demonstrated significant and promising outcomes in managing advanced melanoma, with certain strategies also gaining approval for adjuvant use. Over the past decade, the 5-year survival rate for advanced melanoma patients treated with B-Raf and mitogen-activated protein kinase (MEK) inhibitor combinations or anti-programmed cell death 1 (PD1) monotherapy has markedly improved, rising from <5% to approximately 30%.[22-25] Consequently, there is a pressing need to gain a more comprehensive understanding of the molecular mechanisms underlying the pathogenesis of melanoma. Such insights could pave the way for developing more effective and adaptable treatment modalities, thereby expanding the clinical repertoire for melanoma therapy.

However, there is no research on the impact of UV-associated genes on melanoma prognosis. Based on The Cancer Genome Atlas (TCGA) melanoma database, this study constructed a prognostic model using UV-associated genes to predict the prognosis of melanoma. It also includes drug predictions for 19 genes identified in the model,

providing insights for clinical prognosis assessment and therapeutic selection in melanoma treatment.

2. Methods

2.1. Gene expression data and clinical information of patients

The melanoma cohort was downloaded from the TCGA database.[26] UV-associated genes were downloaded from the UV-related Gene Database, which contains 663 UV-associated genes.[27]

2.2. Differential gene expression (DEG) and gene function enrichment analysis

DEG analysis was conducted using R software version 4.0.2 and the R package "edgeR."[28] Gene ontology (GO) terms were analyzed using the "clusterProfiler" package in the R software.[29] Based on identified protein IDs, GO annotations for proteins were retrieved by mapping them to the UniProt database, enabling functional classification and annotation of proteins. The corresponding proteins were listed for the GO nodes involved in biological process, cellular component, and molecular function, and statistical charts were generated to illustrate the secondary classification of expressed proteins. ClusterProfiler is a powerful package designed for functional enrichment analysis and visualization of gene sets. It supports multiple enrichment analysis methods, including over-representation analysis based on hypergeometric tests and gene set enrichment analysis[30] based on permutation tests. ClusterProfiler can analyze pathways from the GO[31] and Kyoto Encyclopedia of Genes and Genomes (KEGG) databases,[32] as well as user-defined gene sets. First, the gene set of interest was prepared, and then enrichment analysis was performed using functions provided by clusterProfiler. For example, the enrichGO function can be used for GO enrichment analysis, or the enrichKEGG function can be used for KEGG enrichment analysis. These functions provided the enrichment analysis results, including enriched pathways, gene ratios, background ratios, *p*-values, adjusted *p*-values, and *q*-values, among other information.

2.3. Gene signature identification and prognostic model development

We identified 169 genes significantly associated with prognosis ($p<0.05$). Subsequently, we employed the Least Absolute Shrinkage and Selection Operator–Cox regression model, utilizing the "glmnet" and "survival" R packages, to perform variable selection, resulting in the identification of 19 genes to construct a prognostic model. The risk score was computed as follows in Equation I:

Risk score = (Gene 1 × coefficient of Gene 1) + (Gene 2 × coefficient of Gene 2) +… + (Gene 8 × coefficient of Gene 8) (I)

Patients were stratified into two groups based on their risk scores. Survival analysis between the high-risk and low-risk groups was conducted using the Kaplan–Meier method, with statistical significance assessed using a two-tailed log-rank test, where $p<0.05$ was deemed significant. We integrated clinical characteristics with patient risk scores to create nomograms for cancer prognosis prediction. The predictive accuracy of the nomogram was evaluated using the concordance index.

2.4. Analysis of immunological features in melanoma

We used TIMER2.0 (http://timer.cistrome.org/) to analyze immune infiltrates in melanoma.[33] The results were displayed using R software version 4.0.2.

2.5. Mutation analyses of UV-associated prognostic signatures

cBioPortal (http://www.cbioportal.org/)[34-36] was used to analyze the mutation of UV-related prognostic signatures. The cBioPortal database is an international public repository encompassing large-scale cancer research projects such as TCGA and the International Cancer Genome Consortium, integrating cancer genomic data with clinical data. The types of genomic data it consolidates include somatic mutations, DNA copy number alterations, mRNA and microRNA expression, DNA methylation, protein abundance, and phosphoprotein abundance. cBioPortal supports a variety of analyses, but its primary focus is on mutation-related analyses and their visualization. It allows queries for single genes in single cancer types and enables analyses for multiple genes in single cancer types, single genes in various cancer types, multiple genes across multiple cancer types, and cross-cancer genomic projects. In addition, the cBioPortal database supports biological pathway exploration, survival analysis, mutual exclusivity analysis among genomic alterations, selective data downloads, programmatic access, and publication-quality summary visualizations.

2.6. Analysis of single-cell transcriptome sequencing data in melanoma

The analysis of single-cell transcriptome sequencing data was conducted using the CancerSEA database (http://biocc.hrbmu.edu.cn/CancerSEA/).[37] The database enables the exploration of cancer cell heterogeneity at single-cell resolution. This heterogeneity poses a major obstacle to cancer diagnosis and treatment. For instance, within

a tumor, some cancer cells exhibit high proliferative activity, others possess tumor invasiveness and metastatic potential, some display stem cell-like properties, while others remain in a "dormant" or quiescent state. These functionally heterogeneous cancer cells interact through cooperation or competition during tumor evolution, leading to diverse tumor phenotypes. Therefore, it is crucial to comprehensively and thoroughly understand the functional states of cancer cells for advancing cancer research and improving therapeutic strategies.

2.7. Prediction of drug efficacy

We used the connectivity map database for drug prediction of UV-associated genes.[38-40] We believe the associations between genes, diseases, and drugs established through gene expression profiles can assist researchers in drug development. By rapidly comparing gene expression profile data, researchers can identify drugs highly correlated with diseases, infer the primary structures of most drug molecules, and deduce potential mechanisms of action for these molecules.

2.8. Statistical analysis

Statistical analyses were conducted utilizing the R software, version 4.0.2. $p<0.05$ was deemed statistically significant for all statistical evaluations.

3. Results

In this study, we conducted a comprehensive prognostic analysis on 663 UV-associated genes to identify those associated with melanoma patient outcomes. Through rigorous screening, we identified 169 genes significantly linked to melanoma prognosis. Further refinement using the Least Absolute Shrinkage and Selection Operator–Cox method yielded a robust 19-gene prognostic signature for melanoma. These 19 genes – *CD80*, *CRIP1*, *DTL*, *HLA-DRB1*, *IL15*, *OCA2*, *SOD2*, *STAT1*, *TLR2*, *LIF*, *KIT*, *BMI1*, *HSD11B2*, *CDC25A*, *PTH*, *SLU7*, *COL6A3*, *SMAD7*, and *KRT14* – were found to play critical roles in melanoma progression, and their corresponding survival curves are illustrated in Figure 1. The risk score for each patient was calculated using a weighted formula based on the expression levels of these genes, as shown in Equation II.

Risk score = (*CD80* × −0.160969234197251) + (*CRIP1* × −0.0729865857125734) + (*DTL* × 0.0289658462499272) + (*HLA-DRB1* × −0.0408582827147327) + (*IL15* × −0.075201814180893) + (*OCA2* × 0.0160577034585143) + (*SOD2* × −0.0134052166569255) + (*STAT1* × −0.049616959608808) + (*TLR2* × −0.0471253125552539) + (*LIF* × −0.0465743442441398) + (*KIT* × 0.0420186378791114) + (*BMI1* × −0.0129986358809401) + (*HSD11B2* × 0.0911714929889609) + (*CDC25A* × 0.0222044070066866) + (*PTH* × −0.0496764523070364) + (*SLU7* × −0.00399185169578957) + (*COL6A3* × 0.0461021638996901) + (*SMAD7* × −0.0252983631811952) + (*KRT14* × 0.0391890595141816) (II)

This risk score effectively stratified patients into distinct prognostic groups. In addition, the mutation landscape of these 19 genes (Figure 2) provides insights into the genetic alterations associated with melanoma progression. This 19-gene signature enhances our understanding of melanoma biology and offers a potential tool for predicting patient outcomes and guiding personalized treatment strategies.

The prediction results of the prognostic model are shown in Figure 3. Patients with melanoma are divided into high-risk groups according to the expression level of model genes. The high-risk groups have a worse prognosis, and the difference between the two groups is statistically significant ($p<0.0001$). The area under the curve of the receiver operating characteristic curve was 0.615. Based on the nomogram results, age emerged as the primary factor influencing the prognosis prediction of melanoma. The contribution of model scores from race and pathological staging was comparatively similar in proportion.

Figure S1 shows the results of a multi-factor analysis that includes patient clinical characteristics and model risk factors. Figure 4 shows the distribution of risk scores, survival states, and gene expression profiles of genes in the model for skin cutaneous melanoma.

We utilized UV signatures to calculate risk scores for melanoma patients, evaluating each patient sample against the mean expression formula for each gene. Based on these scores, we stratified the TCGA melanoma patient cohort into two distinct groups: high-risk and low-risk. We conducted DEG analysis for the high-risk and low-risk cohorts to further investigate the molecular differences between these groups. This analysis revealed significant variations in gene expression profiles between the two groups. Figure S2 illustrates the GO analysis results of the DEGs in the high-risk and low-risk groups. The analysis identified several signaling pathways that exhibited notable differences between the two groups, including leukocyte cell–cell adhesion, positive regulation of cell adhesion, regulation of leukocyte cell–cell adhesion, and epidermis development. In addition, pathways related to the regulation of inflammatory response, positive regulation of leukocyte cell–cell adhesion, and receptor-ligand activity were significantly enriched. Other pathways with differential activity included signaling receptor activator activity,

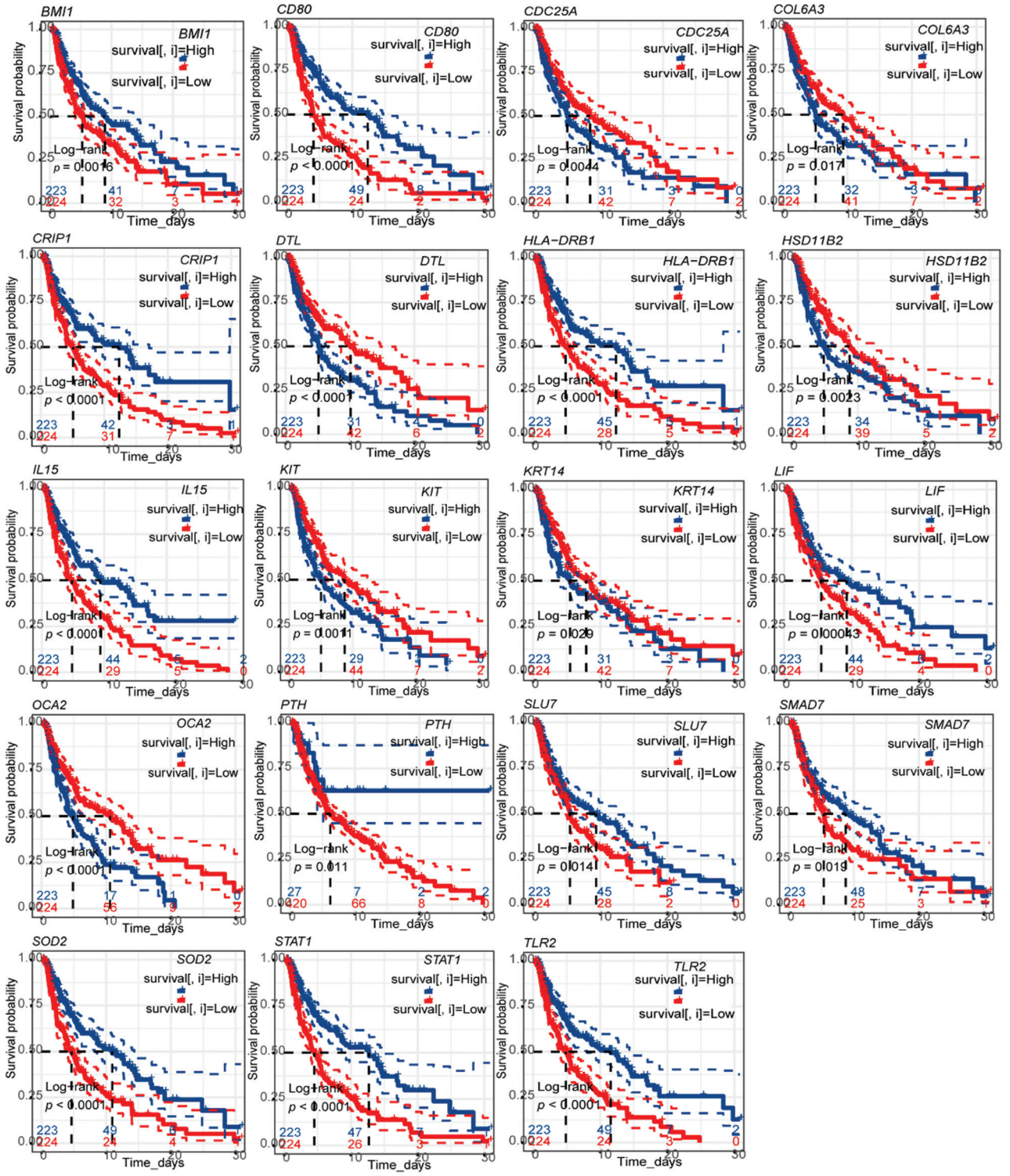


Figure 1. Prognosis of 19-gene signatures. Red represents the high-expression group, blue denotes the low-expression group, and the dashed line indicates the 95% confidence interval.

cytokine receptor binding, cytokine activity, pattern recognition receptor activity, tumor necrosis factor receptor binding, lipopeptide binding, and lipopolysaccharide binding. These findings suggest that the high-risk and

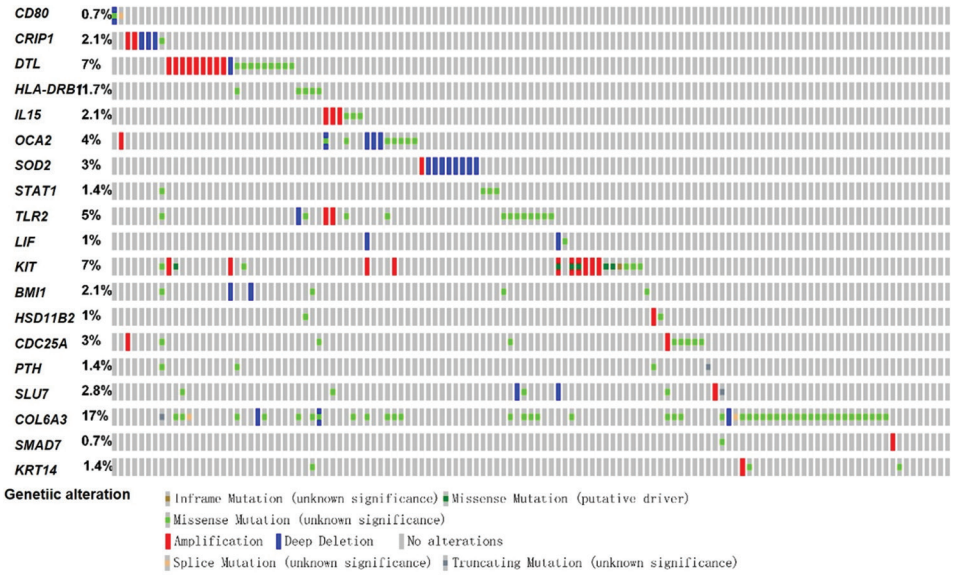


Figure 2. Mutation map of 19-gene signatures

low-risk groups exhibit distinct biological processes and molecular functions, potentially contributing to differences in disease progression and immune response. Identifying these pathways provides valuable insights into the underlying mechanisms driving melanoma heterogeneity and may inform the development of targeted therapeutic strategies tailored to specific risk groups.

3.1. Effects of UV-associated genes on immune infiltration in melanoma

In this study, we employed UV signatures to assess the risk scores of melanoma patients, evaluating each patient sample against the mean expression formula for each gene. Based on these scores, we stratified the TCGA melanoma patient cohort into high-risk and low-risk groups. Subsequently, we conducted a detailed analysis of tumor immune infiltration characteristics for both groups. The results of various immune infiltration analysis methods were consistent, revealing distinct immune profiles between the two groups. In the high-risk group, we observed a significantly higher infiltration proportion of M2 macrophages and activated mast cells, suggesting a potential association with immunosuppressive tumor microenvironments. Conversely, the low-risk group exhibited a markedly higher infiltration proportion of multiple immune cell types, including $CD8^+$ T cells, activated $CD4^+$ memory T cells, activated natural killer cells, M1 macrophage, neutrophils, $CD4^+$ memory T cells, B cells, plasmacytoid dendritic cells, $CD8^+$ central memory T cells, $CD8^+$ effector memory T cells, class-switched memory B cells, myeloid dendritic cells, and memory B cells (Figure 5). These findings indicate a more robust anti-tumor immune response in the low-risk group, characterized by enhanced cytotoxic and memory immune cell activity. The differential immune infiltration patterns between the high-risk and low-risk groups provide valuable insights into the immune landscape of melanoma and may inform personalized therapeutic strategies.

3.2. Characterization of melanoma in single-cell data

In the cluster analysis of two groups of single-cell databases, the genes of the 19-gene signature are highly expressed in tumors and tend to be concentrated in a specific cell population, which is more significant in one of the databases. As shown in Figure 6, UV-associated genes positively correlate with inflammation, invasion, epithelial–mesenchymal transition, cell cycle, DNA damage and repair, cell proliferation, and stemness signaling pathways (Figure 6).

3.3. Expression of model genes in different groups

Due to the multiple and scattered sampling sites, patients with melanoma were divided into the acral and non-acral groups. Figure S3 shows the expression of model genes in different groups. Finally, we performed a drug prediction analysis on 19 UV-associated gene signatures associated with melanoma prognosis. The results are presented in Table S1. These predicted target drugs provide a reference for future melanoma treatment.

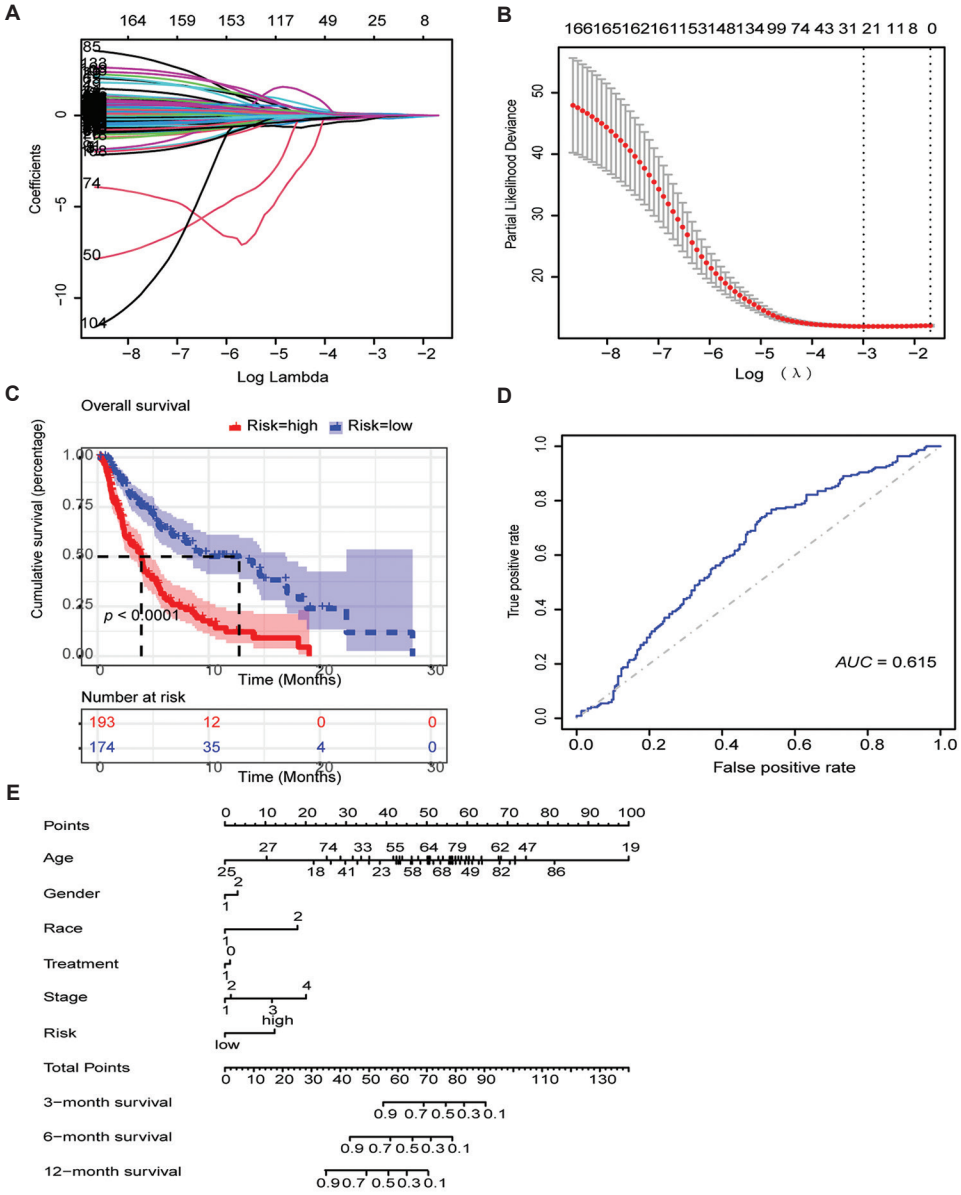


Figure 3. Prognostic model construction and survival analysis based on ultraviolet-associated genes. (A) One-hundred-fold cross-validation for tuning parameter selection in the LASSO model. (B) LASSO coefficient profiles of the most useful prognostic genes. (C) Kaplan–Meier curves of overall survival of The Cancer Genome Atlas Skin Cutaneous Melanoma cohort based on risk score. (D) Receiver operating characteristic curve analysis of ultraviolet gene signature for prediction of overall survival. (E) The nomogram of the models.
Abbreviations: AUC: Area under the curve; LASSO: Least absolute shrinkage and selection operator.

4. Discussion

The carcinogenic effect of UV radiation has long been known to cause DNA strand breaks, gene mutations, and more. The research of UV-associated genes in cancer is also very common, especially in skin cancer. Some studies have reported that UV is related to the formation of melanoma, but its prognostic role in melanoma has not yet been reported.[41,42]

Using the UV-associated gene set as a prognostic model, we found significant differences in prognosis between the high-risk and low-risk groups. Through the GO signaling pathway enrichment analysis of DEGs between high-risk and low-risk groups, we found significant differences in signaling pathways between the two groups. The results show that the infiltration proportion of M2 macrophages and activated mast cells in the high-risk group is higher. In the low-risk group, $CD8^+$ T cells, activated $CD4^+$ memory

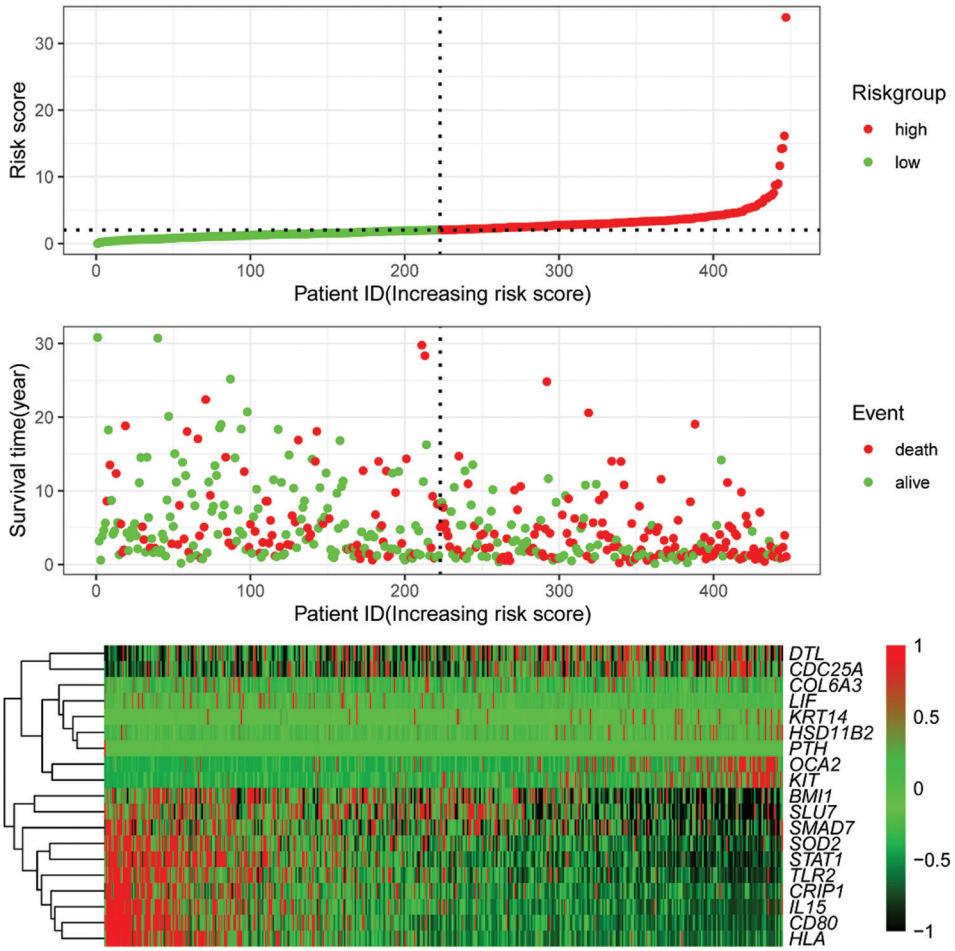


Figure 4. Distribution of risk scores, survival statuses, and gene expression profiles of genes in the model for skin cutaneous melanoma. Red represents high risk, while green signifies low risk.

T cells, activated natural killer cells, M1 macrophage, neutrophils, $CD4^+$ memory T cells, B cells, plasmacytoid dendritic cells, $CD8^+$ central memory T cells, $CD8^+$ effector memory T cells, class-switched memory B cells, myeloid dendritic cells, and memory B cells had a higher infiltration proportion (Figure 5).

The low-risk group demonstrates a better prognosis, which is associated with the enrichment of tumor-killing signaling pathways within the tumor microenvironment. In contrast, the high-risk group is characterized by the activation of pathways that promote tumor initiation and progression. Immune cells play a crucial role in tumor development, especially in determining patient prognosis. UV-associated genes greatly affect immune function, thereby affecting the prognosis of patients.

We analyzed acral and non-acral melanoma data and found that 19 model genes had higher expression levels in non-acral melanoma samples. This difference could be attributed to the large difference in sample size. The number of acral samples in the data is too small, so a larger sample size is needed to support this result.

Clustering analysis of two single-cell databases revealed that UV-associated genes were concentrated in a specific cell population, with this enrichment being more pronounced in one dataset. This indicates that a group of cells in melanoma is very closely related to UV-associated genes, likely representing melanoma cells themselves. These cells may be highly sensitive to changes in UV-associated gene expression, potentially initiating tumorigenesis and contributing significantly to melanoma progression. The positive correlation between UV-associated genes and dry (possibly stemness) signaling pathways in single-cell data supports the idea that these UV-responsive cells may have unique functional states relevant to melanoma initiation and evolution. However, the specific relationship requires further analysis and experiments, such as lineage tracking experiments, for verification.

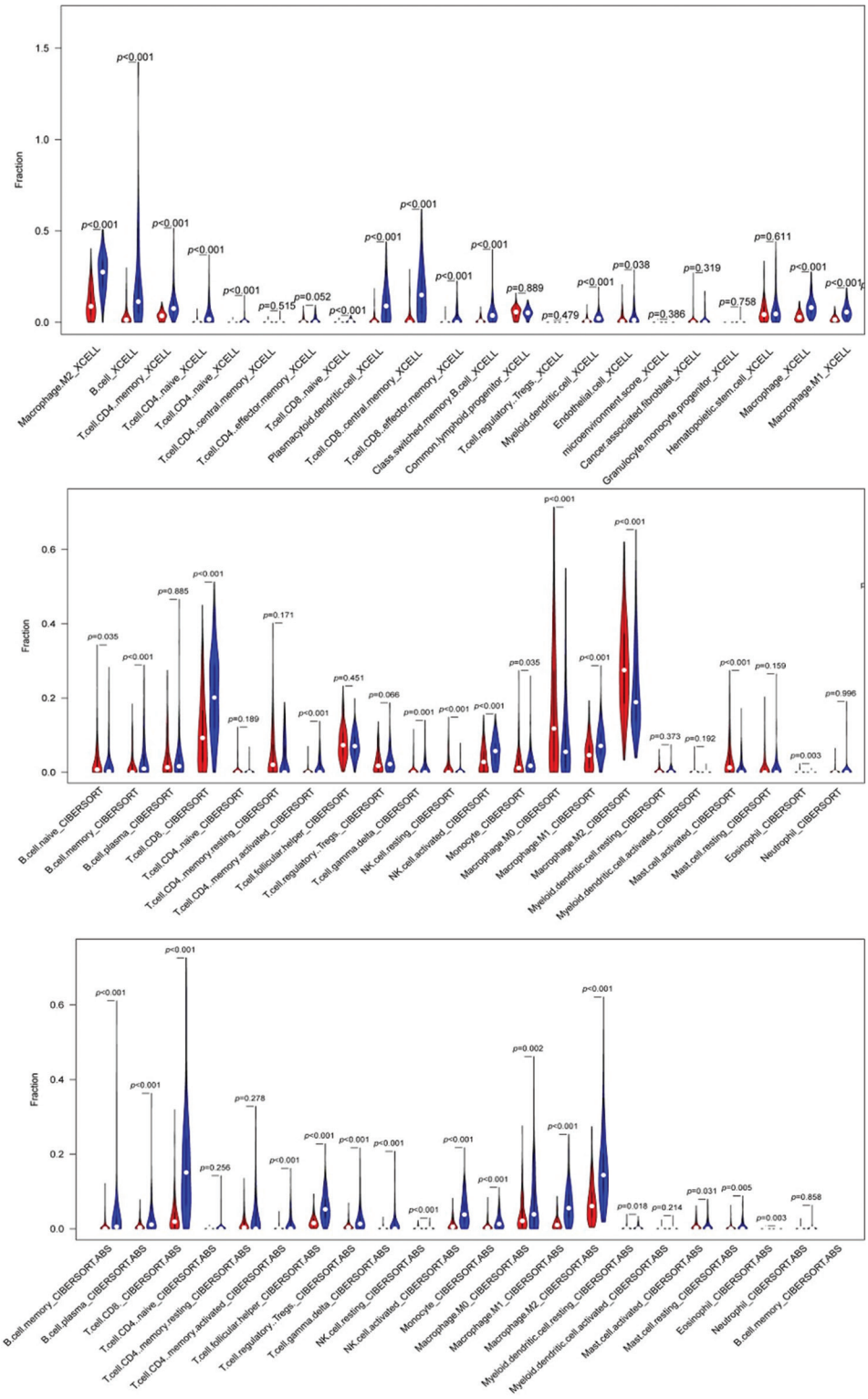


Figure 5. Immunological infiltration analysis between high- and low-risk groups. Red represents the high-risk group, while blue represents the low-risk group. The comparison between the two groups was conducted using a *t*-test. $p<0.05$ was deemed statistically significant.

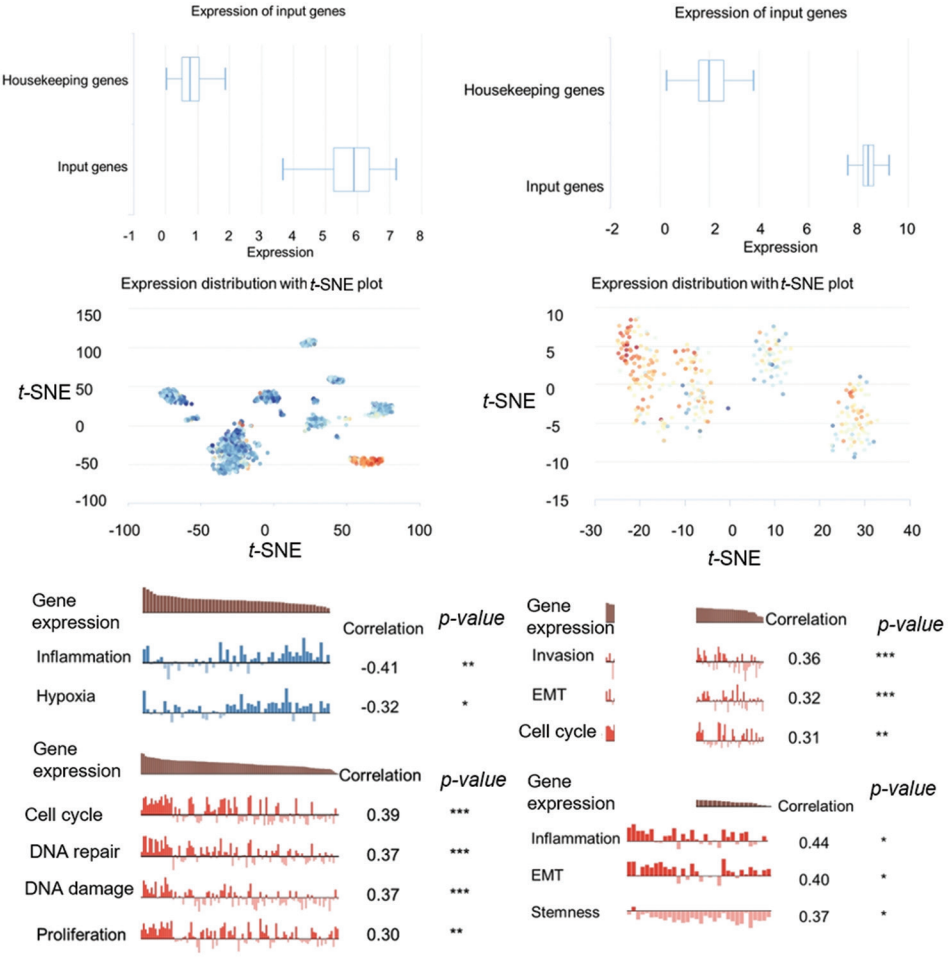


Figure 6. Analysis results of two groups of single-cell sequencing data from the CancerSEA database, EXP0071 and EXP0072. Red represents a positive correlation, while blue signifies a negative correlation. The comparison between the two groups was conducted using a *t*-test. $p<0.05$ was deemed statistically significant.
Abbreviations: EMT: Epithelial–mesenchymal transition; *t*-SNE: *t*-distributed stochastic neighbor embedding.

The main characteristics of melanoma are the dysfunction in both cell proliferation and immune signaling pathways, suggesting that treatment can improve the prognosis of patients by inhibiting tumor cell growth while enhancing immune-mediated tumor destruction. Current clinical trials suggest that immune checkpoint inhibitors have good efficacy in the treatment of melanoma, but the efficacy is low, leaving many patients without effective therapies. Combining immunotherapies or adding other targeted therapies may improve efficacy and patient prognosis. Our drug predictions based on the UV-associated prognostic model genes can provide a valuable reference for clinical treatment. However, extensive experiments are still needed for drug validation and screening.

Melanin production is a defining feature of melanocytes, influenced by a multitude of factors such as genetic predisposition, exposure to UV radiation,[43] and inflammation.[44] A comprehensive understanding of melanogenesis mechanisms is essential for developing innovative preventive and therapeutic approaches for melanoma.[45] Recent studies emphasize the significance of targeting B-Raf, neuroblastoma RAS, and melanocortin-1 receptor in melanoma prevention and treatment. The integration of immunotherapy with targeted kinase inhibitors is gaining prominence as a cutting-edge therapeutic strategy for advanced melanoma.[46]

Since 2010, the U.S. Food and Drug Administration has approved a range of therapeutic drugs and combination regimens for melanoma, marking a transformative era in its treatment. These include immunotherapies, such as ipilimumab, nivolumab, and pembrolizumab, both as monotherapies and in combination (ipilimumab plus

nivolumab), as well as targeted therapies such as vemurafenib and dabrafenib, used alone or in combination with MEK inhibitors (dabrafenib plus trametinib, vemurafenib plus cobimetinib, and encorafenib plus binimetinib). The intratumoral oncolytic herpes virus therapy, talimogene laherparepvec, was also approved. These advancements have led to significant and durable responses in advanced melanoma patients, with some therapies also being utilized in adjuvant settings. Over the past decade, the 5-year survival rate for advanced melanoma patients treated with B-Raf inhibitors, MEK inhibitors, or PD1 inhibitors has risen from <5% to approximately 30%. Despite these breakthroughs, challenges such as low response rates and the development of treatment resistance hinder further enhancement of therapeutic efficacy.[47,48]

Cytokines used in immunotherapy have demonstrated clinical efficacy but are often accompanied by severe adverse events caused by excessive and systemic immune activation. Research has been conducted to address these challenges by engineering a fusion protein consisting of a single, potency-reduced IL15 mutein (IL15m) and a PD1-specific antibody (anti-PD1-IL15m). This immunocytokine is designed to deliver PD1-mediated, avidity-driven IL2/15 receptor stimulation to $PD1^+$ tumor-infiltrating lymphocytes while minimizing the impact on circulating peripheral natural killer cells and T cells. Treatment of tumor-bearing mice with anti-mPD1-IL15m demonstrated potent antitumor efficacy without exacerbating weight loss in B16 and MC38 syngeneic tumor models. Furthermore, in the B16 melanoma model, anti-mouse PD1-IL15m was more effective than an IL15 superagonist, anti-mouse PD-1, or their combination.[47]

Bioinformatics plays a pivotal role in studying gene expression characteristics in melanoma. Through high-throughput sequencing technologies and bioinformatics analysis methods, gene expression patterns closely associated with the occurrence and progression of melanoma can be identified. These patterns include specific gene mutations, DEGs, and changes in gene expression networks. Utilizing these gene expression features as biomarkers, predictive models can be developed. By applying algorithms such as machine learning to analyze patients' gene expression data, it is possible to predict the risk of melanoma, its prognosis, or the response to specific treatments. For instance, by analyzing transcriptomic data from melanoma patients, gene expression features related to tumor invasiveness, metastatic potential, or immune evasion can be identified. These features can serve as diagnostic tools to help physicians identify high-risk patients earlier or as therapeutic targets to guide the development of personalized treatment strategies. In addition, gene expression characteristics can be used to monitor treatment efficacy and disease progression, supporting clinical decision-making. In summary, by integrating multi-omics data and clinical information, bioinformatics can unveil the molecular mechanisms of melanoma and transform gene expression characteristics into effective predictive and diagnostic tools. This advancement improves early detection, precise treatment, and patient management in melanoma.

5. Limitations

This study exclusively utilizes data from the TCGA database, as it represents one of the most comprehensive and largest repositories of cancer genomic data available. However, a notable limitation of this research is the absence of experimental validation for the data-derived results. While prognostic validation is inherently difficult to confirm through experimental data alone, incorporating additional experimental or clinical validation in future studies would strengthen the reliability and translational potential of the findings. This would help bridge the gap between computational predictions and practical cancer research and treatment applications.

6. Conclusion

This study used UV-associated genes to predict melanoma prognosis and stratify melanoma patients, with patients in the high-risk group having a worse prognosis. It investigated the relationship between UV-associated genes and tumor immune infiltration in melanoma patients. It was found that tumor-killing immune cell infiltration in the tumor tissue was lower in the high-risk group compared to the low-risk group.

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Conflict of interest

The authors declare that they have no competing interests.

Author contributions

Conceptualization: Hao Cheng
Formal analysis: Xiaoyun Jiang, Defeng Kong
Methodology: Xiaoyun Jiang, Defeng Kong
Writing – original draft: Xiaoyun Jiang, Defeng Kong
Writing – review & editing: All authors

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data

Data will be made available on reasonable request from the corresponding author.

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