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An overview of melanoma and non-melanoma cancers: An updated review

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***Abstract*---Background:** Skin cancer is the most prevalent cancer in the United States, with melanoma as the fifth most common. Despite melanoma constituting only 1% of skin cancer cases, it is responsible for a disproportionate number of deaths. Non-melanoma skin cancers (NMSC) account for over 5 million cases annually. Public awareness of sunburn and its risks remains low, contributing to high incidences of skin cancer and treatment costs, which have surged significantly in recent years. **Aim:** This review aims to explore emerging biomarkers for melanoma and NMSC to facilitate early detection and risk stratification among high-risk populations. **Methods:** The review analyzes literature on the relationship between ultraviolet radiation (UVR) exposure, genetic mutations, and biomarkers associated with

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melanoma and NMSC development. It focuses on various classes of biomarkers, including those related to susceptibility, exposure, and prognosis. **Results:** UVR exposure is a well-established risk factor for both melanoma and NMSC, leading to mutations, particularly in the TP53 gene. Various susceptibility markers have been identified, including the Fitzpatrick skin phototype classification and the presence of nevi. Emerging biomarkers, such as transcriptomic alterations in melanocytes and the identification of "hyperhotspots" in the genome sensitive to UVR, provide promising avenues for risk assessment. **Conclusion:** The identification and validation of specific biomarkers can enhance early detection strategies for melanoma and NMSC, ultimately aiming to reduce the incidence and mortality rates associated with these cancers. Public health initiatives should focus on improving compliance with UV protection guidelines and promoting awareness of the risks associated with UV exposure.

***Keywords*---**skin cancer, melanoma, non-melanoma skin cancer, ultraviolet radiation, biomarkers, early detection, risk stratification.

Introduction

Approximately one in five individuals in the United States is impacted by skin cancer, rendering it the most prevalent cancer in the country. Excluding non-melanoma skin cancer (NMSC), melanoma ranks as the fifth most common cancer, with forecasts indicating that more than 100,000 new melanoma cases will be diagnosed by the close of 2020. Despite accounting for merely 1% of all skin cancer cases, melanoma is responsible for a substantial proportion of skin cancer-related fatalities, with projections suggesting that nearly 7,000 individuals will succumb to this disease by year-end [1]. Annually, over 5.4 million NMSC cases are addressed across more than 3.3 million patients in the United States [2]. In spite of persistent efforts to enhance public awareness regarding sunburn and the associated risks of skin cancer, sunburn continues to be exceedingly prevalent among American adults. Data from the Centers for Disease Control (CDC) reveal that the prevalence of sunburn remains alarmingly high, with 50.1% of all American adults and 65.6% of white individuals aged 18-29 reporting at least one instance of sunburn each year [3]. While sunburn typically resolves several days post-exposure, repeated occurrences lead to cumulative genetic and epigenetic damage in skin cells. Although sunburn is a well-documented risk factor in the development of skin cancer, there are often prolonged intervals—sometimes spanning decades—between sunburn incidents and the appearance of visible skin tumors. Molecular alterations induced by sunburn can persist for years to decades in sun-exposed pre-malignant skin, potentially culminating in malignant transformation over time. Conventional skin cancer screening methodologies, including dermoscopy, are advantageous for tumor detection; however, they frequently fail to identify tumors at early stages due to their limitations in detecting cancer-associated molecular changes before visible tumors manifest [4-6]. Presently, the assessment of skin damage from sun exposure is primarily based on the minimal erythema dose (MED), which quantifies the quantity of ultraviolet radiation (UVR) necessary to elicit visible

skin reddening within 24 hours of exposure. The duration required to reach MED is contingent on the level of UVR exposure. However, MED is not an optimal indicator, as substantial UV-induced molecular harm can transpire following sub-MED UV exposure [7, 8]. Sunburn is predominantly preventable, and implementing preventive measures represents the most economically viable strategy to decrease the incidence of skin cancer and associated treatment expenditures [9]. A critical factor contributing to the persistent rise in sunburn and skin cancer rates is the insufficient public adherence to UV protection guidelines [10]. This low compliance is partially due to the absence of quantifiable risk information that can aid in educating and motivating at-risk patients. With the escalating incidence of skin cancers and the accompanying treatment costs, there exists an urgent imperative for more effective strategies for prevention and early detection, aimed at mitigating healthcare expenditures, morbidity, and mortality. The average annual expenditure for skin cancer treatment surged by 125%, from $3.6 billion between 2002 and 2006 to $8.1 billion from 2007 to 2011 [11]. In contrast, the average annual cost of treating other cancer types rose by only 25%, from $63.7 billion to $79.7 billion during the same timeframe.

Biomarkers have been employed across various types to furnish insights into disease development, progression, and prognosis. Over time, there has been considerable interest in the advancement of biomarkers to enhance disease prevention and facilitate early detection. Molecular signatures possess the capability to identify diseases at an early stage and stratify individuals according to their susceptibility. Given the delay between sunburn and the onset of skin cancers, alongside the challenges inherent in early detection, there is considerable interest in biomarker-based assessments for risk evaluation, aiming to bolster skin cancer prevention and reduce diagnostic delays. As the costs associated with treatment significantly surpass those of photoprotective strategies, there is substantial interest in both primary prevention and screening initiatives for high-risk populations, which could ultimately lower incidence rates and enhance early skin cancer detection. Prognostic biomarkers will enable the identification of these high-risk groups for targeted screening and preventive measures. This discussion will explore emerging biomarkers for melanoma and NMSCs that may facilitate risk stratification within the population and inform targeted primary and secondary prevention efforts for early detection and treatment.

Risk Factors and Emerging Biomarkers for Melanoma and NMSC

Exposure to ultraviolet radiation (UVR) that leads to sunburn is a well-recognized risk factor for the development of both melanoma and non-melanoma skin cancer (NMSC) [12-15]. Biomarkers are specific molecules whose detection or evaluation yields information regarding a disease that extends beyond the conventional clinical parameters collected by healthcare professionals [16]. While several FDA-approved multi-gene panel tests exist for risk prediction and diagnosis across various cancers [17], a standardized FDA-approved biomarker test for risk stratification remains unavailable. Numerous studies have previously attempted to identify genes responsive to UV exposure [18-23]. However, a consensus UV biomarker panel is yet to be established due to significant variations among earlier studies and the absence of cross-validation for candidate biomarker genes.

This discussion will encompass various classes of biomarkers, including those indicative of susceptibility, exposure, prognosis, progression, and metastasis.

UV Radiation as a Risk Factor:

UVA and UVB radiation are mutagenic, primarily through the induction of dimerization and structural breaks in DNA, with these so-called UV signature mutations frequently observed in melanoma skin cancers. Approximately 76% of primary melanomas and 84% of metastatic melanomas exhibit such signature mutations, with further mutational burden (occasionally utilized for classification) correlating with the extent of sun exposure [24, 25]. These UV signature mutations are also present in NMSC, with actinic keratoses (AK), squamous cell carcinomas (SCC), and basal cell carcinomas (BCC) all linked to mutations in the TP53 gene, a well-known tumor suppressor, with over 70% of these mutations attributable to UVR [26-28]. Research has demonstrated that these somatic mutations can also be detected in normal, sun-exposed skin devoid of malignancy. For instance, a study employing deep targeted sequencing of biopsies from sun-exposed eyelid epidermis revealed that, on average, each cell harbored over 10,000 somatic mutations, the majority of which bore a UV signature mutation [29]. Positively selected mutations were identified in 18% to 32% of normal skin cells. Consequently, aged, sun-exposed skin can contain a considerable proportion of oncogenic mutations while retaining the normal functionality of the epidermis, thereby supporting the multi-stage model of carcinogenesis [30, 31]. These findings raise concerns regarding the reliability of mutation-based biomarkers for skin cancer risk assessment.

Markers of Susceptibility:

Susceptibility markers for the development of NMSC and melanoma encompass skin type and the presence of heritable mutations. The Fitzpatrick skin phototype classification system is the most widely utilized method for assessing skin cancer risk, categorizing skin pigmentation on a scale from I to VI, ranging from light to dark, and incorporating an individual's self-reported tendency to tan or burn, with skin type I being prone to burn easily and tan poorly [32]. Research indicates that the Fitzpatrick classification system serves as a more robust predictor of skin cancer risk compared to pigmentary phenotypes, including hair, eye, and skin color [33]. However, a limitation of this classification is its potential inaccuracy for individuals with darker skin tones [34, 35]. The quantity of common and atypical nevi has also been identified as an independent risk factor for melanoma development [36]. A meta-analysis revealed that having over 100 common nevi, in contrast to fewer than 15, correlates with a relative risk of 6.85 for developing melanoma, while the presence of five atypical nevi, compared to none, was similarly associated with a relative risk of 6.36 [36]. Multiple heritable mutations are associated with the risk of NMSC and melanoma. For instance, individuals with xeroderma pigmentosum possess mutations in nucleotide excision repair genes, resulting in an over 1000-fold increased risk of developing skin cancer [37]. Those with basal cell nevus syndrome exhibit heritable mutations in the tumor suppressor gene PTCH [38]. While family history represents an important risk factor for melanoma, these familial cases account for only 1% to 2% of all cutaneous melanoma cases [39]. Specifically, the cyclin-dependent kinase CD4

gene and the cyclin-dependent kinase inhibitor gene CDKN2A significantly elevate risk in 20% to 40% of high-risk families [39].

Measures of Exposure to UV Radiation:

Several biomarkers can assess exposure to UV radiation, including the minimal erythema dose (MED), alterations in gene expression, and levels of microRNA. MED currently serves as the principal indicator of skin sun damage; however, it is both insensitive and inadequate as significant UV-induced molecular damage may occur following sub-MED UV exposure [7, 8]. Additional measures of UVR exposure include the quantity of benign nevi present during childhood, a recognized risk factor for melanoma development [36]. Furthermore, photoproducts such as cyclobutane pyrimidine dimers and pyrimidine (6-4) pyrimidone, formed as a consequence of UVR, can also serve as indicators of acute UV damage. Research has demonstrated that acute UVR exposure can lead to significant transcriptomic instability, affecting thousands of genes [8, 18]. UVR upregulates the expression of genes involved in cellular stress and inflammation, including protein tyrosine phosphatase receptor type E, thrombospondin-1, inducible costimulatory ligand, galectins, Src-like adaptor protein, IL-10, and CCR7 [19]. RNA sequencing has identified significant dysregulation of 2,186 genes in human skin 48 hours post-UVB exposure [18]. This dysregulation includes numerous chemokines and cytokines such as interleukin 6 and 24, CCL3, CCL20, CXCL1, CXCL2, CXCL3, CXCL5, COX2, and various members of the keratin gene family [18].

Alterations Induced by Ultraviolet Radiation in Epidermal Melanocytes

Research on the effects of ultraviolet radiation (UVR) on epidermal melanocytes revealed significant changes at the transcriptomic level. Out of 47,000 transcripts analyzed, 84 genes (48 of known identity) exhibited over a two-fold suppression due to UVR, while 99 genes (57 of known identity) were induced by more than two-fold as a result of UV exposure. Notably, several genes associated with the TP53 pathway were highlighted, including the cell cycle regulator CDKN1A, Wnt pathway regulator DKK1, receptor tyrosine kinase EPHA2, growth factor GDF15, ferredoxin reductase (FDXR), p53-inducible protein TP53, transcription factor ATF3, DNA repair enzyme DDB2, and beta-adrenergic receptor ADBR2. Additionally, UVR has been linked to epigenetic modifications. A study utilizing chromatin immunoprecipitation to analyze histone 3 lysine 27 acetylation (H3K27ac) revealed that UVR led to a genome-wide decrease in H3K27ac levels, accompanied by localized increases in certain regions. A significant correlation was observed between the reduction in H3K27ac and decreased gene expression observed 72 hours post-UV exposure, but not at the four-hour mark. Another recent investigation focused on the genomes of human fibroblasts and melanocytes to identify regions with increased sensitivity to UVR. The study identified 2,000 “hyperhotspots” within the human genome that exhibited up to 170 times greater sensitivity to UVR than average genomic regions. These hyperhotspots, which are prone to cyclopyrimidine dimer formation—the primary photoproduct resulting from UV exposure—were predominantly found in melanocytes. They were distributed throughout the genome and were particularly frequent near genes that regulate cell proliferation. Researchers are currently

exploring these hyperhotspots as potential biomarkers for assessing skin cancer risk, as a significant contributor to skin cancer development is prior UV exposure. Given the accumulation of cyclopyrimidine dimers in these hyperhotspots, they may serve as objective indicators of UV exposure in small skin samples [40-41].

Biomarkers for Risk Stratification of Pre-Cancerous Lesions

Solar ultraviolet radiation (UVR) plays a pivotal role in the etiology of squamous cell carcinoma (SCC) and its precursor lesions, actinic keratoses (AKs). It is estimated that approximately 65% of SCC cases develop from AKs, with a progression rate from AK to SCC estimated at less than 5% [42]. Consequently, there is an increasing focus on creating robust and sensitive assays to identify high-risk AKs and SCCs. One investigation analyzed the expression of p53, E-cadherin, Snail, Slug, and Twist in AK lesions to pinpoint biomarkers that correlate with clinical progression and regression of AKs. Results indicated that p53 expression levels were significantly elevated in clinically observable AKs compared to regressed variants. Additionally, clinically apparent AKs exhibited markedly reduced levels of membrane E-cadherin, a known indicator of epithelial-to-mesenchymal transition. The transcriptional repressors Snail, Slug, and Twist were also found to be upregulated in AKs in contrast to normal sun-exposed skin [43]. Ongoing research aims to identify genes that can effectively distinguish between high-risk AKs and less aggressive lesions that are unlikely to progress to SCCs. This differentiation will enable the identification of benign AKs, thereby preventing unnecessary interventions in the 95% of AKs that do not evolve into malignant cancers.

Markers of Disease Progression

Biomarkers are also utilized to evaluate the risk of disease progression and metastasis. Phosphorylated signal transducers and activators of transcription (pSTAT1 and pSTAT3) have been implicated in the pathogenesis and advancement of melanoma. The proportion of pSTAT3-positive melanocytes correlates with the degree of atypia in nevi [44]. Notably, pSTAT1 and pSTAT3 exhibit opposing biological functions, and the pSTAT1/pSTAT3 ratio has been explored as a potential prognostic marker, with elevated ratios in tumor tissues indicating better overall survival outcomes for patients [44]. Furthermore, treatment with interferon-alpha (IFNα) has been shown to enhance this ratio in a dose-dependent manner [44]. Various molecular markers have been identified that may characterize distinct stages of melanoma development. The melanoma inhibitory activity (MIA) protein is selectively expressed in melanoma cells rather than in melanocytes and plays a critical role in tumor development and progression [45]. Serum MIA levels have been employed to differentiate metastatic melanoma from non-metastatic melanoma and from control groups comprising patients with dysplastic nevi or basal cell carcinoma (BCC) without melanoma [46]. MIA facilitates melanoma progression and metastasis by interacting with fibronectin and integrin, disrupting cell-matrix adhesion and promoting the migration of melanoma cells to other tissues [45]. Additionally, MIA influences melanoma development by modulating the expression of transcriptional regulators, such as MITF and PAX3, which are integral to melanoma pathogenesis [47].

Emerging interest has also centered on the role of microRNA (miRNA) in melanoma pathogenesis, progression, and metastasis. MiRNAs are small (22-nucleotide) single-stranded non-coding RNAs that negatively regulate the expression of over 60% of the human genome. Circulating miRNAs hold promise as biomarkers for the early detection of melanoma [48]. Initially identified in peripheral circulation in 2008, miRNAs are transported within microparticles or complexed with RNA-binding proteins or lipoproteins, which shield them from degradation by ribonucleases [49]. Several studies have highlighted the potential of miRNAs in differentiating melanoma patients from healthy individuals. A specific panel comprising 16 circulating miRNAs that were either upregulated or downregulated demonstrated an ability to distinguish between these groups with 95% specificity and 98.9% sensitivity [50]. MiRNA expression levels may also serve as indicators of the likelihood of melanoma metastasis. One study compared miRNA levels among primary non-metastatic melanomas, primary metastatic melanomas, and metastases, revealing significant differences in the expression of miR-145, miR-203-3p, and miR-205-5p. Notably, miR-145-5p and miR-203-3p exhibited significantly reduced expression in metastatic samples compared to primary non-metastatic tumors. Additionally, lower expression of these miRNAs correlated with aggressive tumor characteristics, including Breslow thickness greater than 1 mm, elevated Clark level, ulceration, and a mitotic rate exceeding $1/mm^2$ [51].

Role of Primary Prevention in Reducing Skin Cancer Incidence

Given that ultraviolet radiation (UVR) is a significant risk factor for skin malignancies, minimizing exposure can mitigate the onset of the genetic and epigenetic alterations associated with these conditions. The critical role of prevention is underscored by studies indicating that UVR is linked to nearly 70% of non-melanoma skin cancers (NMSCs) and 90% of melanomas [52-54]. This approach serves as a complementary strategy alongside UV biomarkers for both primary prevention and cost-effective health management. Public health initiatives have been launched worldwide, with new campaigns emerging in the United States as well. Established campaigns like SunSmart® in Australia have demonstrated significant success, resulting in decreased melanoma incidence rates [55]. It is estimated that the SunSmart® program alone has prevented 50,000 skin cancers and 1,400 fatalities, yielding savings exceeding $92 million [56]. Although public health campaigns have commenced in the United States, the effectiveness of these programs may not become evident for several decades [57]. The primary focus of these campaigns is the promotion of sun-safe practices, which include the application of broad-spectrum sunscreens with a sun protection factor (SPF) of 30 or higher, as well as the use of protective clothing. Regular sunscreen application has been associated with long-lasting effects on the incidence of primary melanomas (hazard ratio [HR] 0.50, 95% confidence interval [CI] 0.24-1.02, P = .05) extending up to 10 years [58], and early childhood use is similarly linked to reduced risk in adulthood [59]. Despite the demonstrated efficacy of primary prevention efforts, there are currently no established guidelines in the United States regarding sunscreen use for the prevention of skin malignancies. This absence of governmental endorsement may be attributed to the inconsistent outcomes of earlier studies. Various factors have been suggested to explain these mixed findings, including increased sun exposure

due to a false sense of security from perceived protection [60], inadequate application of sunscreen [61], limited duration of follow-up [62], and the delayed effects of prior sun exposure [62]. Additionally, the human papillomavirus (HPV) vaccine has been shown to prevent and treat keratinocyte carcinomas [63, 64]. One investigation assessed the prophylactic effect of the HPV vaccine on the development of keratinocyte carcinoma in two patients with a history of multiple squamous cell carcinomas (SCCs) and basal cell carcinomas (BCCs). One patient experienced an average of 12 new SCCs and 2.25 new BCCs annually prior to vaccination, which decreased to 4.44 SCCs and no new BCCs per year post-vaccination, representing a 62.5% reduction in SCCs and a 100% reduction in BCCs. The second patient had an average of 5.5 new SCCs and 0.92 new BCCs per year before vaccination, with subsequent reductions to 1.84 SCCs and no BCCs, indicating a 66.5% reduction in SCCs and a complete elimination of BCCs [63, 64]. These findings suggest that the HPV vaccine could serve as a promising preventive intervention for individuals at high risk of keratinocyte carcinomas. However, the current body of research primarily comprises case series and reports, indicating a need for more robust evidence regarding the vaccine's efficacy for primary prevention on a population level. The widespread implementation of the HPV vaccine for cervical cancer prevention may provide an unintentional natural experiment, offering valuable insights into its effectiveness in reducing skin malignancies.

Biomarkers for Targeted Screening of High-Risk Patients

Ultraviolet (UV) biomarkers are instrumental in identifying high-risk individuals for secondary prevention via targeted screening. This is particularly significant in light of the absence of established guidelines for skin cancer screening in the United States. Both the 2016 United States Preventive Services Task Force (USPSTF) and a recent Cochrane review concluded that there is insufficient evidence to endorse routine skin cancer screening [65]. Implementing risk stratification can help avoid screening in low-risk populations, which may lead to inflated treatment costs without substantial mortality benefits due to the overdiagnosis of melanoma and other skin cancers, as evidenced in other cancer types such as breast and prostate cancers [66]. Specialists advocate for screening among populations deemed high risk, as per the Melanoma Prevention Working Group's recommendations in response to the USPSTF's conclusions [67]. Targeted screening of selected patient groups may facilitate the early diagnosis of melanoma, enhancing quality of life and lowering treatment costs. The advantages of a nationwide screening initiative have already been demonstrated in Europe through population-based studies [68]. For instance, the skin cancer screening campaign (SCREEN) launched in Schleswig-Holstein, Germany, in 2003 resulted in a nearly 50% reduction in melanoma mortality [69, 70]. However, following the program's conclusion in 2008, mortality rates reverted to baseline levels. Supporting these findings, research conducted at the University of Pittsburgh revealed that annual full-body skin examinations in individuals aged over 35 led to earlier melanoma detection, with identified lesions being 50% thinner than those found in unscreened patients [71]. Currently, screening for high-risk patients is endorsed in countries such as Australia, New Zealand, the Netherlands, and the UK [67]. An Australian study indicated that high-risk populations may face a melanoma risk as high as 18.2% over four years [72].

Participants in this study met at least one of four criteria: (a) a personal history of at least one invasive melanoma and dysplastic nevus syndrome; (b) a personal history of at least one invasive melanoma alongside a family history of at least three first- or second-degree relatives with melanoma; (c) a personal history of two or more primary invasive melanomas, with at least one occurring within the decade preceding recruitment; or (d) confirmed mutations in the CDKN2A or CDK4 genes. Identifying and monitoring high-risk patients significantly improves outcomes through early detection and proves to be cost-effective [73-74]. Biomarker-based tests can effectively delineate this high-risk group and facilitate targeted screening efforts.

Conclusion

Melanoma and non-melanoma skin cancers remain significant public health concerns in the United States, necessitating ongoing research and innovative prevention strategies. The reviewed literature highlights the critical role of ultraviolet radiation (UVR) in the pathogenesis of these cancers, establishing a clear link between sun exposure, genetic mutations, and skin cancer development. Emerging biomarkers offer promising insights into disease risk stratification, aiding in the identification of individuals at heightened risk for developing melanoma and NMSC. The exploration of biomarkers extends beyond traditional risk factors, suggesting that molecular and genetic markers can enhance the accuracy of risk assessments. The identification of UV-sensitive "hyperhotspots" within the genome provides a new perspective on how UVR contributes to carcinogenesis, paving the way for the development of targeted screening protocols. Furthermore, the potential for biomarkers to serve as indicators of UV exposure emphasizes the need for integration of biomarker assessments into routine dermatological evaluations. Despite advancements in understanding the molecular underpinnings of skin cancer, there remains a substantial gap in public adherence to UV protection measures. The high rates of sunburn among the population indicate an urgent need for comprehensive public health campaigns aimed at educating individuals on the risks of UV exposure and the importance of protective strategies. Ultimately, addressing the rising incidence of melanoma and NMSC will require a multifaceted approach that combines public education, innovative biomarker research, and enhanced screening protocols. By fostering greater awareness and understanding of skin cancer risks, it is possible to improve early detection and reduce the morbidity and mortality associated with these malignancies. This review underscores the importance of continued research and the need for effective public health initiatives to combat the increasing burden of skin cancer.

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نظرة عامة على سرطان الجلد الميلانيني وغير الميلانيني - مراجعة محدثة.

الملخص:

الخلفية :يعتبر سرطان الجلد أكثر أنواع السرطان انتشارًا في الولايات المتحدة، حيث يحتل سرطان الميلانوما المرتبة الخامسة من بين الأنواع الشائعة. على الرغم من أن سرطان الميلانوما يمثل 1٪ فقط من حالات سرطان الجلد، إلا أنه مسؤول عن عدد غير متناسب من الوفيات. تمثل سرطانات الجلد غير الميلانينية أكثر من 5 ملايين حالة سنويًا. لا يزال الوعي العام بحروق الشمس ومخاطرها منخفضًا، مما يساهم في ارتفاع معدلات الإصابة بسرطان الجلد وتكاليف العلاج، التي زادت بشكل كبير في السنوات الأخيرة.

الهدف :تهدف هذه المراجعة إلى استكشاف المؤشرات الحيوية الناشئة لسرطان الميلانوما و NMSCلتسهيل الكشف المبكر وتصنيف المخاطر بين الفئات السكانية عالية المخاطر.

الطرق :تحلل المراجعة الأدبيات حول العلاقة بين التعرض للأشعة فوق البنفسجية (UVR) والطفرة الجينية والمؤشرات الحيوية المرتبطة بتطور الميلانوما و .NMSCتركز على فئات مختلفة من المؤشرات الحيوية، بما في ذلك تلك المتعلقة بالاستعداد، والتعرض، والتشخيص.

النتائج :يُعتبر التعرض للأشعة فوق البنفسجية عامل خطر معروفًا لكل من الميلانوما وNMSC، مما يؤدي إلى الطفرات، وخاصة في جين .TP53تم تحديد علامات استعداد مختلفة، بما في ذلك تصنيف نوع بشرة فيتزباتريك ووجود الشامات. توفر المؤشرات الحيوية الناشئة، مثل التغيرات النسخية في الخلايا الصبغية وتحديد "نقاط الهايبرهوتسبوت" في الجينوم الحساسة للأشعة فوق البنفسجية، مسارات واعدة لتقييم المخاطر.

الخلاصة :يمكن أن يُعزز تحديد وتوثيق مؤشرات حيوية معينة استراتيجيات الكشف المبكر عن الميلانوما وNMSC، بهدف تقليل معدلات الإصابة والوفيات المرتبطة بهذه السرطانات. يجب أن تركز المبادرات الصحية العامة على تحسين الالتزام بإرشادات الحماية من الأشعة فوق البنفسجية وتعزيز الوعي بالمخاطر المرتبطة بالتعرض للأشعة فوق البنفسجية.

الكلمات المفتاحية :سرطان الجلد، الميلانوما، سرطان الجلد غير الميلانيني، الأشعة فوق البنفسجية، المؤشرات الحيوية، الكشف المبكر، تصنيف المخاطر.