Advances in Ophthalmology Practice and Research 4 (2024) 98–105

Contents lists available at ScienceDirect

Advances in Ophthalmology Practice and Research

journal homepage: www.journals.elsevier.com/advances-in-ophthalmology-practice-and-research

Full Length Article

A UV-related risk analysis in ophthalmic malignancies: Increased UV exposure may cause ocular malignancies

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ARTICLE INFO

Keywords:
Ultraviolet radiation
Eyelid malignancies
Conjunctival melanoma
Uveal melanoma
Ocular surface squamous neoplasia

ABSTRACT

Purpose: To explore the role of ultraviolet radiation (UVR) in the occurrence and development of various ocular malignancies.
Methods: In this article, we retrieved ocular malignancy data from the Global Cancer Observatory (GCO) and performed correlation analysis with the global UV index and sunshine duration. We searched for associated studies using the following databases: Embase, Pubmed, Cochrane Library, and Google Scholar. We conducted the literature by searching the Mesh terms denoting an exposure of interest ("UV radiation", "ultraviolet rays", and "ocular malignancies", All studies included are published until December 30, 2023 without language restrictions.
Results: The mechanisms and epidemiological statistics of UVR on the onset and progression of eyelid malignancies are the most studied and clear. The role of UVR in conjunctival melanoma is similar to that in eyelid melanoma. The relationship between uveal melanoma and UVR is controversial, however, it may have at least a certain impact on its prognosis. UVR causes ocular surface squamous neoplasia by further activating HPV infection.
Conclusions: UVR is a decisive risk factor for ocular malignancies, but the incidence of ultraviolet-induced tumors is also affected by many other factors. A correct and comprehensive understanding of the mechanisms of UVR in the pathogenesis of ocular malignant tumors can provide patients with more effective and selective immune regulation strategies.

1. Introduction

Many ocular diseases are associated with acute or cumulative ultraviolet (UV) exposure of the eyes.[1] The UV spectrum can be further divided into three bands: UV-A (315–400 nm), UV-B (280–315 nm) and UV-C (100–280 nm).[2] The UV ray that reaches the earth through the absorption of the ozone layer and can enter the eye consists mainly of UV-A and a small amount of UV-B.[3] Ultraviolet rays are carcinogenic in many previous studies.[1,4,5] The incidence of ocular malignancies is increasing, and whether this rising trend is related to acute and chronic sun exposure. This is one of the hot topics in clinical prevention and public health management.

Ocular malignant tumors can seriously damage vision and even threaten life. Therefore, it would be ideal if preventive measures could be found to ultimately reduce the risk of developing ocular malignancies. This article analyzes and evaluates the association between ocular malignancies and UV exposure. We analyzed the correlation between ocular malignancies and ultraviolet radiation (UVR) through the database, elaborated on the influencing factors of UVR-induced different ocular malignant tumors and reviewed the latest progress in the mechanisms of UVR-induced tumors from different aspects.

2. Interactions between UVR and the eye

Eye and skin penetrate and filter UV rays differently. In the skin, both UV-A and UV-B radiation penetrate the dermis; UV-A penetrates more deeply than UV-B.[6] The eye has a physical protection mechanism that does not exist in the skin, and its sensitivity to ultraviolet rays differs

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https://doi.org/10.1016/j.aopr.2024.04.001
Received 19 December 2023; Received in revised form 8 March 2024; Accepted 2 April 2024

from that of the skin. Table 1 shows the UV absorption levels of different eye parts for different wavelengths.[7] Thus, although most of the more damaging UV light is absorbed by the structures in front of the eye, a very small fraction of it reaches the retina and choroid.[8]

3. Methods

Global epidemiological data on ocular malignancies were extracted from the database of the Global Cancer Observatory (GCO) (gco.iarc.fr). Ocular melanoma and non-melanoma incidence rates were adjusted to the Age-standardized rate (ASR) per 100000 inhabitants. Data on average UV index and annual sunshine hours in different countries are derived from data from the World Health Organization's online website. As mentioned in the following, data from other sources were also used. According to the United Nations Statistics Division, countries are further divided into geographical regions. We classify countries in North America, Europe, and Oceania with populations mainly of European ancestry as Caucasian countries, while we classify countries in Asia, South America (due to genetic admixture), and Africa as non-Caucasus.

IBM SPSS Statistics 28 (IBM Corp, Armonk, USA) was used for statistical analysis. All graphs were constructed using GraphPad Prism 8.0.1 (GraphPad Software, San Diego, CA, USA). All data were verified for normal distribution using the Shapiro-Wilk test. We performed Pearson correlation analysis on the ocular malignancy incidence with UV index and annual sunshine duration. Considering the incidence of ocular melanoma in Caucasians, we further performed Pearson correlation analysis on Caucasian countries. $P < 0.05$ was considered statistically significant.

4. Results

We calculated the annual distribution of the UV index in key regions in recent years. (Fig. 1). Countries close to the equator, such as Singapore and Kenya, have the highest UV index, with annual averages of about 11.5 and 11.7. Some mid-latitudes, such as Australia, South Africa, and Argentina in the southern hemisphere, have a more varied seasonal distribution of UV index, with high levels in summer (9) and low levels in winter (2). Areas far from the equator, such as Russia, have relatively low UV index, with a maximum of 5 throughout the year. In global regions, the ASR of non-melanoma has a positive correlation with UV index. ($P = 0.012$, $r = 0.416$) (Fig. 2A) However, the relationship between the ASR of melanoma and UV index is not significant. ($P = 0.372$) (Fig. 2B) Further analysis of Caucasian race regions showed that the ASR of non-melanoma and melanoma are positively correlated with UV index. ($P < 0.001$, $P = 0.032$, respectively) Meanwhile, the ASR non-melanoma is highly linearly correlated with UV index, and the ASR melanoma ASR is significantly linearly correlated with UV index. ($r = 0.801$, $r = 0.448$, respectively) (Fig. 2C and D) The ASR of Non-melanoma was also positively correlated with sunshine duration ($P = 0.011$), and there was a significant linear relationship ($r = 0.519$). while melanoma ASR was not significantly correlated ($P = 0.160$) (Fig. 2E and F). Globally regionally, the development of ocular non-melanoma is more closely related to UVR and is positively affected by it. The effect of UVR is greater in Caucasians. In Caucasian regions, the ASR of ocular non-melanoma significantly correlates positively with UV intensity and duration. However, ocular melanoma ASR is not significantly affected by UV duration but is still closely related to UV intensity.

5. Discussion

It is known that the incidence of basal cell carcinoma (BCC), squamous cell carcinoma (SCC), melanoma of the eyelid skin or conjunctiva, and ocular surface squamous neoplasia (OSSN) has been correlated with UV exposure to varying degrees in several previous studies.[6,9–13] There is also some support in the literature for UV exposure as a risk factor for the development of intraocular malignant tumors such as uveal melanoma.[14] Therefore, based on UV radiation and distribution and the incidence of ocular malignancies, it can be seen that the association is proportional to a certain extent. Our analysis results show that ocular non-melanoma malignancies are related to UV index, while ocular melanoma is more related to skin color-dependent UV in Caucasians.

5.1. Molecular changes in ocular malignancies in the context of UVR influence

5.1.1. Melanoma

Melanocytes are essential for protecting the skin from the harmful effects of UV radiation. Paradoxically, melanocytes are the precursor to the deadliest form of melanoma.[15] Thus, the relationship between melanoma and UV exposure has a complex two-sided mechanism. The upstream of the key cell proliferation pathway of melanoma is the mitogen-activated protein kinase (MAPK) pathway, and the two mutated genes involved in this pathway are NRAS mutations and BRAF mutations.[8,16] UV exposure early in life is associated with the development of BRAF mutant melanomas, whereas NRAS mutations are more commonly associated with high UV exposure in later life.[9] UV ray causes characteristic mutations at the DNA nucleotide level, i.e., UV mutations, embodied in the mechanism of DNA photodamage, including: Direct absorption of UVB photons by DNA bases result in the production of photoproducts, i.e., the cyclobutane pyrimidine dimer (CPD, in the majority) and the 6-pyrimidin-4-pyrimidinone photoproduct (6–4 (PP)), in the minority), which are formed in the same DNA strand between two neighboring pyrimidine sites (TT, CT, TC, CC) between two neighboring pyrimidine sites in the same DNA strand, which in turn give rise to C→T and CC→TT mutations during cellular repair, hence the term UV mutation.[17] Most of the UV mutations act on the MAPK pathway, and then participate in the pathogenesis of melanoma (Fig. 3).

Table 1
Absorption of UVR of different wavelengths by various parts of the eye.

UV	Wavelength range (nm)	Content	Clinical Ocular Correlation	Absorption Structure (%)				
				Cornea/ Conjunctiva	Aqueous/ Iris	Lens	Vitreous	Retina
UVA	315–400	Not absorbed by ozone layer	UVA radiation passes through the cornea, but lens absorption prevents much of the radiation from reaching deeper eye structures	45 (at 320 nm) 37 (at 340 nm) 34 (at 360 nm)	16 (at 320 nm) 14 (at 340 nm) 12 (at 360 nm)	36 (at 320 nm) 14(at 340 nm) 12 (at 360 nm)	1 (at 320 nm) 1 (at 340 nm) 2 (at 360 nm)	< 1
UVB	280–315	Substantial portion absorbed by ozone layer	The cornea transmits ultraviolet radiation with wavelengths exceeding 300 nm. UVB has the greatest potential for retinal phototoxicity and choroidal photocarcinogenicity.	92 (at 300 nm)	6 (at 300 nm)	2 (at 300 nm)	0	0
UVC	100–280	Most portion absorbed by ozone layer	Cornea completely blocks UVC radiation	100	0	0	0	0

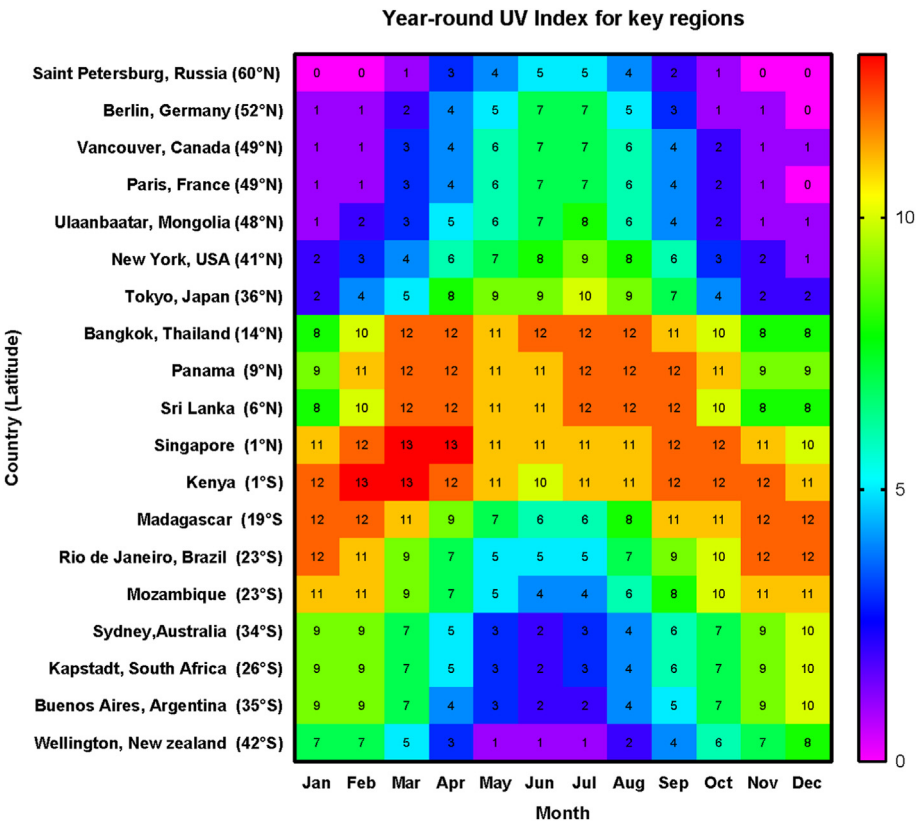

Fig. 1. Year-round UV index for key regions.

5.1.1.1. BRAF-mutant melanoma. BRAF mutations occur in approximately 50% of melanomas, and they occur primarily at or around codon 600 of exon 15.[18] In a population-based case series from North Carolina, USA, cases of BRAF (+) cutaneous melanoma were found to be associated with high estimated UV irradiance at ages 0, 10, and 20 years, i.e., a strong association of BRAF mutations with UV exposure early in life.[9] A pooled analysis of 5700 melanoma cases confirmed that childhood sunburn is a risk factor for melanoma development.[19] Similarly, Amaya Viro et al. verified through mouse experiments that melanocytes expressing BRAF ^{V600E} are susceptible to low-dose UVR-driven proliferation and pigmentation that mimics mild sunburn, concluding that UV ray accelerates BRAF ^{V600E}-driven melanoma genesis.[20]

5.1.1.2. NRAS-mutant melanoma. NRAS mutations have been previously reported to be UVB-independent genetic events that occur early in melanoma evolution, whereas p16 ^{INK4a} loss is usually associated with malignant progression.[21] However, a mouse experiment suggests that UV light, in synergy with NRAS^{61R} alone, drives melanoma formation 80% faster than controls (p16 INK4a-deficient mice), suggesting that NRAS activation, rather than p16 ^{INK4a} loss, is the major cooperating factor in sunlight-induced melanoma.[22]

5.1.1.3. Other UV-related melanocyte mutations. In addition to the most common NRAS mutations and BRAF mutations, the third most common mutation in UVR-exposed melanoma is the activating mutation (P29S) in RAC1, a typical UVR-related mutation and a driver mutation in melanoma.[23] The common oncogene in melanoma is phosphatidylinositol-3, 4,5-trisphosphate-dependent RAC exchange factor 2 (PREX2).[24] PREX2 mutations are also more common in body parts exposed to UVR. PREX2 works by promoting the PI3K/AKT pathway. MAPK pathways interact to promote melanoma cell proliferation.[24]

5.1.1.3.1. Eyelid melanoma and conjunctival melanoma. Both the eyelid skin and conjunctiva are directly exposed to UVR, and exhibit a high burden of the typical C→T mutational signature that represents UV damage to DNA, some researches suggests that conjunctival melanoma is genetically similar to eyelid melanoma.[13,25] NRAS mutations are common in human UV-exposed cutaneous melanomas but are rare in mucosa.[12,26] Similarly, conjunctival melanomas, like eyelid melanomas, typically have a high mutational load, and specific mutations are associated with UV exposure.[27] Therefore, there is no doubt that UV exposure has an effect in this type of melanoma.

5.1.1.3.2. Intraocular melanoma. Uveal melanoma (UM) is the second most common melanoma (after skin) and the most common intraocular malignancy.[8,28] The incidence of intraocular melanoma is different from that of eyelid skin melanoma due to UVR. The cornea can completely block UVR with wavelengths below 300 nm, while the lens can absorb part of UVA. As age-related clouding of the lens occurs, cataracts develop in the lens and implanted UV-protective intraocular lenses can absorb UVB radiation. However, the transparent lens does transmit a small but potentially large amount of dangerous radiation to the retina.

Based on previous studies, the epidemiologic and biological evidence linking UV radiation from sunlight to the pathogenesis of uveal melanoma is weak and even contradictory.[14] The quality and quantity of melanin determines the degree of sensitivity of melanocytes to UV damage, which correlates with uveal melanoma risk. Thus, light iris color and light skin color are risk factors for the development of uveal melanoma.[29] Compared with cutaneous melanoma, choroidal melanoma has different UV-related morbidity. However, there is also research result showing that the distribution of uveal melanoma origins is related to the dose distribution of solar radiation on the retinal sphere.[30]

Unlike the incidence of cutaneous melanoma, which has obvious latitudinal differences, the incidence of uveal melanoma in Australia and New Zealand, where the incidence of cutaneous melanoma is very high, is not much different from that in Europe [31]. There is a clear north-south gradient in the incidence of eyelid melanoma in Norway, with incidence rates in the south being three times higher than in the north. No such

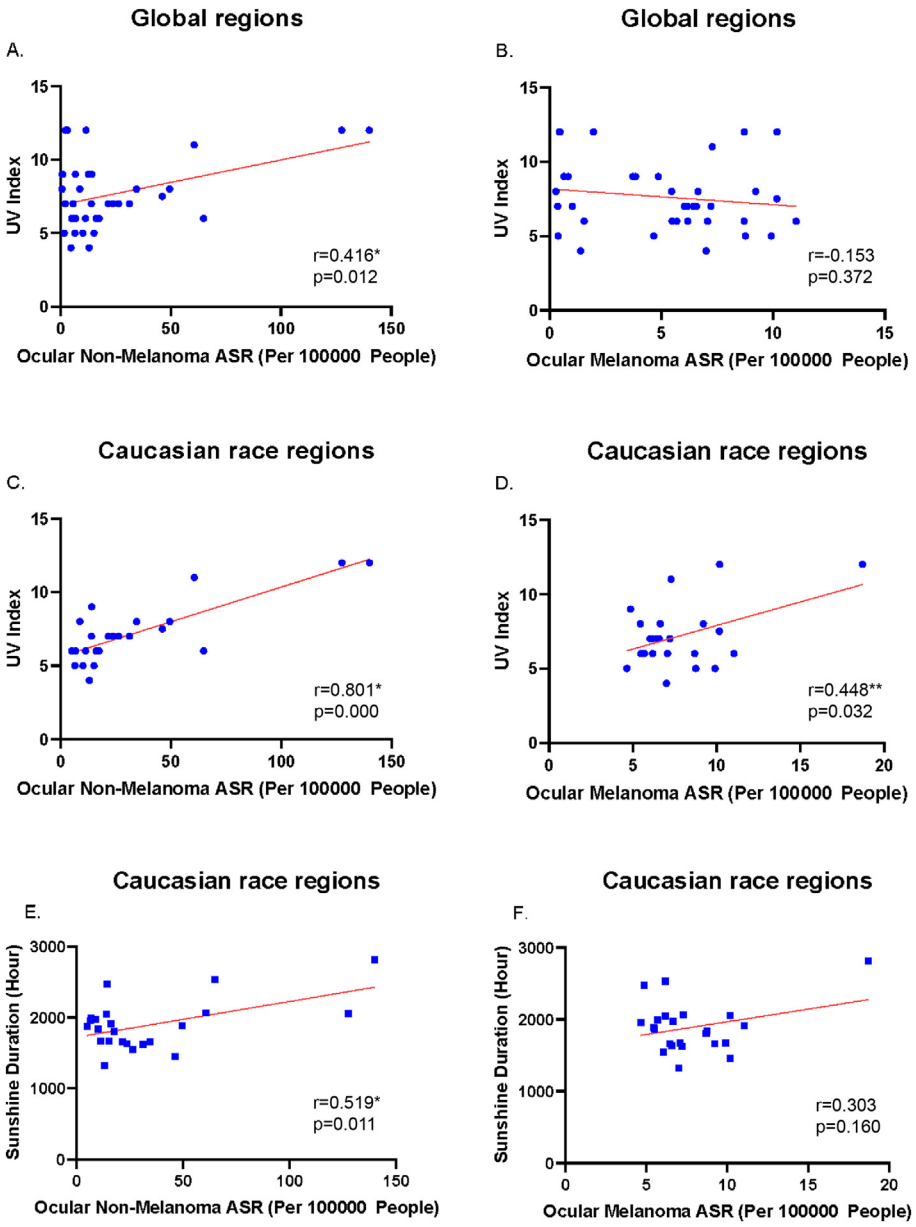

Fig. 2. (A) In global regions, Pearson correlation between UV index and ocular non-melanoma ASR; (B) In global regions, Pearson correlation between UV index and ocular melanoma ASR; (C) In the Caucasian race regions, Pearson correlation between UV index and ocular non-melanoma ASR; (D) In the Caucasian race regions, Pearson correlation between UV index and ocular melanoma ASR; (E) In the Caucasian race regions, Pearson correlation between sunshine duration and ocular non-melanoma ASR; (F) In the Caucasian race regions, Pearson correlation between sunshine duration and ocular non-melanoma ASR.

gradient was found in uveal melanoma.[32] Interestingly, however, latitude was a prognostic factor for uveal melanoma, with a higher incidence of mortality associated with uveal melanoma in competing risk analyses in patients who were born in the southern region or moved >1 degree south between birth and diagnosis.[31]

UM has a uniquely low mutational burden and, unlike cutaneous melanoma, is associated with GNAQ/11 mutations at least 80% of the time and is generally not associated with UVR changes despite acting on the same MAPK pathway as BRAF.[33] However, every cross-linked mutation and every common point mutation in BRAF is associated with UV-related mechanistic changes. These findings support the hypothesis that the etiology of a significant minority of UM may be more dependent on UV light than previously recognized.[34] Past ratio-ratio data suggest that measures to avoid sunlight can reduce the risk of UM, despite the lack of conclusive evidence that UVR plays a pathogenic role.[35]

5.1.2. *Non-melanoma*

Basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) have been classified as "non-melanoma skin cancers" (NMSC). UV-induced NMSC is mostly related to direct DNA damage and induction of inflammatory response.[36] Exposure of NMSC to UVB is initially associated with an inflammatory response characterized by increased blood flow and vascular permeability leading to edema and erythema, neutrophil infiltration of the dermis, induction of pro-inflammatory cytokines and ROS production.[37] Inflammatory cells such as neutrophils can be influential tumor promoters, and they and other phagocytes induce DNA damage in proliferating cells by producing reactive oxygen species and nitrogen. Additionally, these cells mediate damage by producing arachidonic acid derivatives, including prostaglandins and leukotrienes, which cause damage associated with UVB-induced cutaneous inflammatory responses.[38] Recent studies have also shown that reaction intermediates such as those produced after UVB exposure may also lead to mutations in genes such as p53, a tumor suppressor gene that has been shown to play an important role in multistep UV-induced tumorigenesis.[39] Unlike UVB, UVA must first react with non-DNA chromophores (e.g., melanin) in the skin to generate ROS (reactive oxygen species , ROS), and UVA-mediated DNA damage occurs indirectly through oxidative stress. Singlet oxygen and other ROS react with guanine and produce a variety

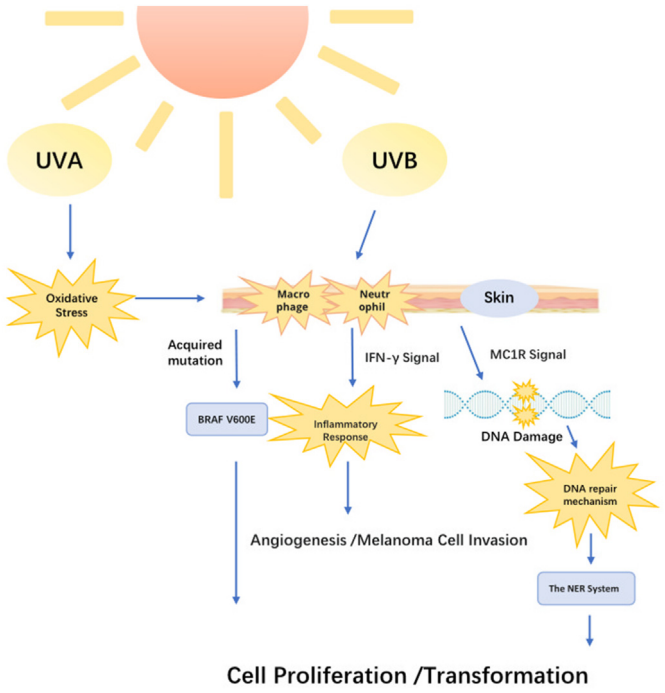

Fig. 3. The Effect Pathway of UVR on Ocular Melanoma
CPDs: cyclobutane pyrimidine dimers; **NER:** Nucleotide Excision Repair; **BRAF:** V-raf Murine Viral Oncogene Homolog B1.

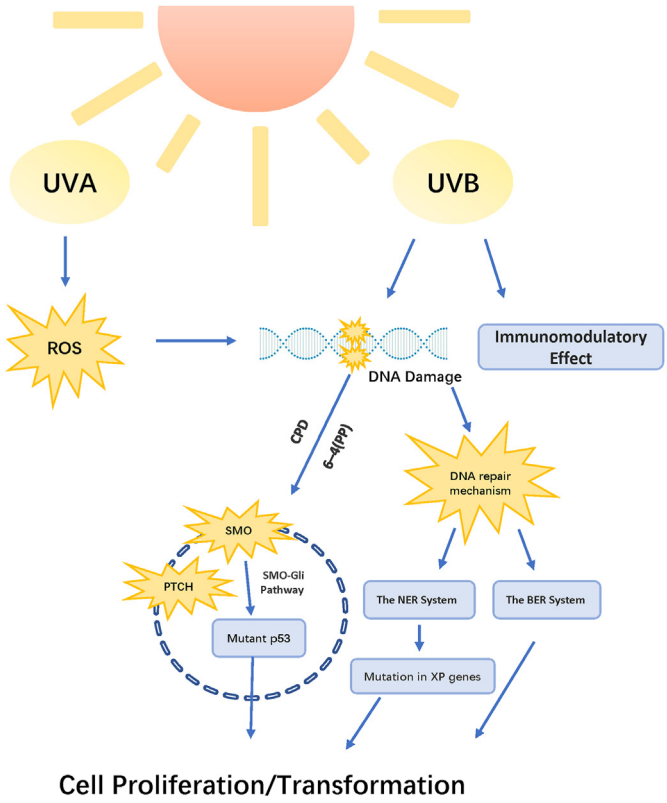

Fig. 4. The effect pathway of UVR on ocular Non-melanoma
ROS: Reactive oxygen species; **CPD:** Cyclobutane pyrimidine dimers; **6–4(PP):** 6-Pyrimidine-4-pyrimidone photoproducts; **NER:** Nucleotide excision repair; **BER:** Base excision repair.

of DNA changes, including the mutagenic 7, 8-dihydro-8-oxoguanosine (8-oxoG).[40] Recently, studies have shown that cyclobutane pyrimidine dimers (CPDs) are the major lesions in UVA-induced DNA damage, supporting a mutagenic mode of action similar to UVB.[41] (Fig. 4).

However, there appear to be considerable biological differences between basal cell carcinoma and squamous cell carcinoma, the major forms of nonmelanoma, and attempts should be made to address each form separately.

5.1.2.1. Eyelid basal cell carcinoma. Basal cell carcinoma of the eyelid is now the most common eyelid skin malignancy worldwide, and UV exposure has been shown to be a key predisposing risk factor for BCC development.[42,43] A latency period of 20–50 years is typically observed between UV damage and clinical onset of BCC.[8] BCC occurs most commonly in adults, especially older adults, but rarely in adults under 50 years of age.[44] According to several epidemiological studies, the incidence of basal cell carcinoma is less related to cumulative sun exposure over a lifetime and may be more related to intermittent (recreational) exposure and childhood exposure.[45]

The pigmentation profile of BCC determines the skin's response to UVR and is controlled by many genes or genetic variants.[46] The melanocortin 1 receptor (MC1R) gene (chromosome 16q24.3) has been documented as one of the genes identified as contributing to phenotypic variation in human hyperpigmentation (hair color, skin color, and tanning ability). It is expressed on melanocytes and regulates true melanin synthesis by binding to α-melanocyte stimulating hormone (α-MSH).[47] Studies have shown that melanocytes with a nonfunctional MC1R (due to a loss-of-function mutation) exhibit increased sensitivity to the cytotoxic effects of UVR in vitro.[48] Single nucleotide polymorphisms in other hyperpigmentation genes, including the human type II oculocutaneous albinism-related gene (OCA2) and the acanthamoeba signaling protein (ASIP) gene, have been associated with BCC risk.[49] In another study of variants in various pigmentation genes in European populations, variants in the ASIP and tyrosinase (TYR) loci were associated with BCC.[50] Epidermal growth stimulates the patched (PTCH) protein gene in the Hedgehog pathway, and PTCH mutations are mainly UV-specific mutations and have also been shown to be mutated in more than 90% of BCCs.[51]

5.1.2.2. Squamous cell carcinoma. Chronic UV exposure has been recognized as a main etiologic agent causing approximately 90% of SCC.[11] The most critical steps in the occurrence of UV-induced SCC are the inactivation of p53, the production of ROS, and the activation of COX-2 [39]. Mutations in the tumor suppressor p53 appear to be an early step in SCC tumorigenesis.[52] The p53 gene is a direct target of UVR, and specific mutations have been found in the coding sequence that result in reduced DNA binding and transcriptional activity.[40] Meanwhile, UVR is known to increase the expression of COX-2 in human skin, and COX-2 is overexpressed in chronic UVB-irradiated skin and UVB-induced SCC.[53] Extrinsic apoptosis is induced by the death ligands TNF-a, CD95L/FasL or TRAIL (TNF-related apoptosis-inducing ligand), which interact with their respective death receptors TNF-R1, CD95, TRAIL-R1 and TRAIL-R2 binding. Recent mouse experiments have found that ultraviolet light regulates death ligand levels to a certain extent, but its exact role in tumorigenesis is unclear.[54]

5.1.2.3. Ocular surface squamous neoplasia. Many studies have confirmed that solar ultraviolet radiation is the main causative factor of ocular surface squamous cell tumors (ocular surface squamous neoplasia, OSSN). Epidemiological studies have shown a linear relationship between OSSN incidence and distance from the equator.[55] Newton et al. found that the geographical distribution of OSSN is highly correlated with environmental ultraviolet dose levels. For every 10° increase in latitude, the incidence of OSSN decreases by 49%. For example, in Uganda, the annual incidence of OSSN patients is 12×10^{-6}; in the UK, the annual incidence is 0.2×10^{-6}.[56] EC.Sun et al. also found that the association between UVB exposure and OSSN rates ($\beta = 2.25$; $r = 0.58$)

was as strong as that of eyelid squamous cell carcinoma (β = 2.73; r = 0.62).[57]

UV affects multiple mechanisms in the pathogenesis of OSSN. HPV infection is an important factor in the pathogenesis of OSSN. Exposure to UVB can cause local and systemic photoimmune suppression, thereby activating latent HPV and participating in the pathogenesis of OSSN.[58] Epidermal growth factor receptor (EGFR) is known to regulate keratinocyte proliferation, differentiation, survival, and is overexpressed in malignancies.[59] UVR activates EGFR family members, including Erbb2 (human epithelial growth factor receptor 2 (HER2)/neu), and EGFR also coordinates UVB-induced matrix metalloproteinases (MMP) expression, including MMP-1 and -3.[60] Compared with normal ocular surface tissue, MMP-1 and -3 expression levels are higher in OSSN tissue.[61] When exposed to UVB, conjunctival epithelial cells exhibit increased expression of MMP-1 and MMP-3, and increased MMP activity disrupts intercellular adhesion and promotes carcinogenesis and tumor invasion into surrounding tissues.[62]

5.2. Differences in UV exposure

Although we have described a large number of UVR-induced mechanisms in the development of ocular malignancies, the dose of UVR, the period of exposure, and the causes of susceptibility to UVR vary for different ocular malignancies.

The risk of eyelid melanoma is associated with intermittent and long-term exposure to the sun, and its frequency is closely related to skin composition, color, and geographic region.[63] Conjunctival melanoma is also caused by direct exposure to UVR like eyelid melanoma. Studies have found its incidence is also closely related to the degree of ultraviolet exposure.[13] There is a lack of clinical evidence on whether there is a dose relationship between ultraviolet exposure and the occurrence of uveal melanoma. However, a previous German study suggested that ultraviolet exposure is a risk factor for uveal melanoma, especially in acute intermittent exposure.[64] The relationship between eyelid squamous cell carcinoma and OSSN and ultraviolet rays is reflected in decades of long-term accumulation of UVR.[65] However, most epidemiological studies on basal cell carcinoma indicate that unlike squamous cell carcinoma, which is directly related to cumulative sun exposure, the association between basal cell carcinoma and the amount or timing of an individual's sun exposure appears more complex. The role of recreational or "intermittent" sun exposure during childhood or adolescence (considered a critical period for tumor development) appears to be particularly important and is a strong risk factor for basal cell carcinoma. Infrequent, intense, and intermittent sun exposure during childhood and adolescence (especially before age 20 years) increases the risk of BCC more than more continuous exposure to similar doses over the same period.[10]

The effects of UV exposure are also related to factors such as a population's susceptibility to UVR. Table 2 summarizes UV-related susceptibility factors for ocular malignancies from multiple regional epidemiological surveys.[66–69] Our summary supports the development of ocular malignancies in part by the production of UV-induced DNA damage, suggesting a link between solar radiation and the development of this tumor. Therefore, public awareness should be increased about the benefits of wearing UV protection glasses in addition to skin sunscreen when exposed to the sun.[8]

Table 2
Susceptibility factors of different ocular malignancies to UV rays.

Types of ocular malignancies	Risk factors associated with UVR sensitivity
Eyelid melanoma	Skin scarring and localized erythema Severe blistering sunburn
Conjunctival melanoma	Similar to eyelid melanoma
Uveal melanoma	Transparent lenses in Children and Young Adults Nordic ancestry, family history of melanoma Light iris color (Blue eyes are most at risk) Chronic occupational UV exposure Fair skin color, Freckling as a child, Nevi on the upper arms, burns to the eyes, Usage of sunlamps
Eyelid basal cell carcinoma	Bowen's disease (As-BD) Number of severe sunburns in lifetime Skin scarring and localized erythema
Eyelid squamous cell carcinoma	People with xeroderma pigmentosum Bowen's disease (As-BD) Occupational UV exposure at low latitudes Number of severe sunburns in lifetime Skin scarring and localized erythema
Ocular surface squamous neoplasia	Precancerous skin lesions (actinic keratosis) Pterygium HIV seropositivity, HPV-related diseases

6. Conclusions

Ocular malignant tumors are vision-threatening and even life-threatening diseases, and their causes and mechanisms remain unclear. Its early diagnosis is difficult and often delayed. Therefore, studying possible risk factors and pathogenic mechanisms is worthy of efforts. As a risk factor for ocular malignant tumors, ultraviolet rays play a crucial role in tumor-related gene mutations, microenvironmental changes, and immune system disorders. But the incidence of UV-induced tumors is also affected by several other factors, such as general characteristics, UV ray source, and other relevant environmental factors. In addition, excessive ultraviolet irradiation directly or indirectly induces skin DNA damage, leading to mutations in related proto-oncogenes and tumor suppressor genes as well as changes in inflammatory responses, ultimately leading to the occurrence and development of tumors. However, the understanding of UV-induced ocular malignancies is still not comprehensive and complete. Its relationship with tumor-related genes, immune regulation, and inflammatory responses requires further study to provide more effective and selective immunomodulatory strategies for patients with ocular malignancies occurring in exposed areas.

Study approval

Not Applicable.

Author contributions

The authors confirm contribution to the paper as follows: Conception and design of study: KY, LH; Data collection: XJ; Analysis and interpretation of results: XJ, YG, AR; Drafting the manuscript: XJ, XL, WF; All authors reviewed the results and approved the final version of the manuscript.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

Thanks to all the peer reviewers and editors for their opinions and suggestions.

Abbreviations

UVR ultraviolet radiation

OSSN	ocular surface squamous neoplasia
BCC	basal cell carcinoma
SCC	squamous cell carcinoma
UM	uveal melanoma
OCA2	the human type II oculocutaneous albinism-related gene
MAPK	mitogen-activated protein kinase
EGFR	epidermal growth factor receptor
MC1R	melanocortin 1 receptor
Erbb2	human epithelial growth factor receptor 2
MMP	matrix metalloproteinases
CPD	cyclobutane pyrimidine dimer

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