



# ROLE OF SUNSCREEN IN SKIN CANCER PREVENTION

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## 1. INTRODUCTION

The skin is the largest organ of the human body, accounting for 16% of the body weight. It serves various functions, including protection, excretion, synthesis, and temperature regulation. Additionally, the skin is the outermost organ of the body, directly interacting with physical, chemical, and biological agents from the external environment. Therefore, the skin is an organ that constantly changes and renews to adapt to external conditions. These external factors play a significant role in the pathogenesis of many skin diseases, with numerous studies highlighting the relationship between ultraviolet (UV) rays and skin cancer.<sup>1,2</sup>

Skin cancer is among the most common cancers in humans, categorized into two main groups: non-melanoma skin cancer and melanoma skin cancer. According to Globocan statistics in 2020, non-melanoma skin cancer ranks 5th among new cases of all types of cancer. However, this statistic is often underestimated because many cases of skin cancer in the early stages may be clinically misdiagnosed as benign lesions and treated with conventional lesion removal without biopsy.<sup>3</sup>

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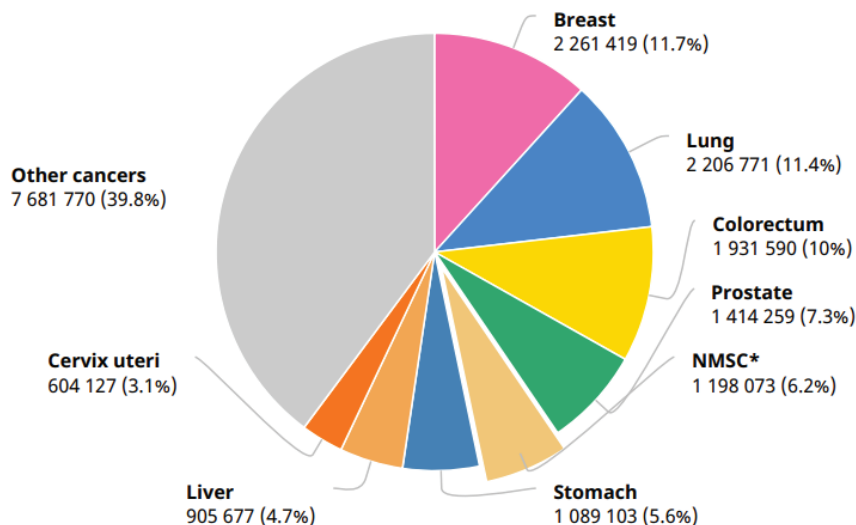
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Number of new cases in 2020, both sexes, all ages

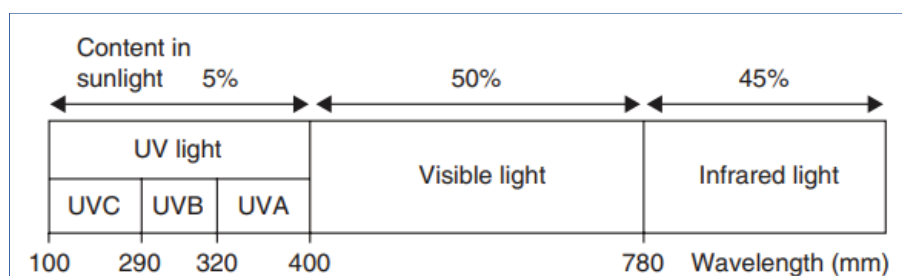


**Figure 1. Statistics of new global cancer cases in 2020. Non-melanoma skin cancer ranks 5th. \*: possibly more in reality**

NMSC: non-melanoma skin cancers

## 2. THE ROLE OF UV RADIATION (UV) IN PATHOPHYSIOLOGY OF SKIN CANCER

Sunlight hitting the Earth consists of a spectrum of electromagnetic waves, which is divided into three main groups: ultraviolet (UV), visible light, and infrared rays. All three groups have effects on human skin. Ultraviolet rays, characterized by high energy, play a significant role in skin carcinogenesis. On the other hand, visible light and the primary infrared rays cause biological stimuli and thermal effects.<sup>4</sup>



**Figure 2. The spectrum of electromagnetic waves from the sun on the skin<sup>4</sup>**

Ultraviolet rays account for only 5% of the total spectrum of electromagnetic radiation from the sun to the Earth. These rays are divided into three smaller groups based on wavelengths: UVC (100 - 290nm), UVB (290 - 320nm), and UVA (320 - 400nm). UVC is entirely absorbed by the ozone layer, while UVB is absorbed up to 95% by the ozone layer. UVA, however, is less absorbed by the ozone layer and can penetrate through clouds and glass doors.<sup>1</sup>



Skin cancer has a complicated pathogenesis. Extrinsic factors act on tumor suppression genes or tumor proliferation genes, altering the activity of these genes and leading to a loss of cell proliferation control and the formation of tumors. Some genes with tumor suppressor roles include Rb, P53, INK4, PTEN, APC, MADR2, while Cyclin D1, KRAS, BRAF, MITF play a role in tumor proliferation. The three most common types of skin cancer, basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and melanoma skin cancer, are associated with UV radiation in the pathogenesis. The P53 gene, which controls programmed cell death and cell cycle control, is the most studied gene in the pathogenesis of skin cancers.<sup>5,6</sup>

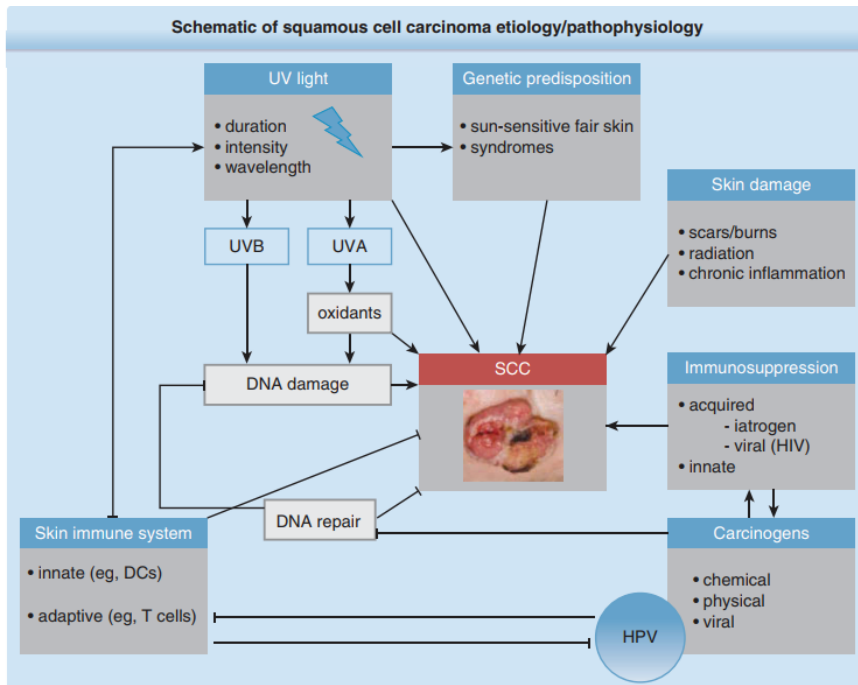
**Basal cell carcinoma (BCC)**

The activation of the sonic hedgehog (SHH) signaling cascade plays a key role in the pathogenesis of basal cell carcinoma (BCC). Additionally, UV-induced point mutations in the

P53 gene have been reported to be associated with 50% of BCC cases. Another study revealed numerous gene mutations involved in the pathogenesis of skin cancer, with 85% of them related to the SHH pathway, including PTCH1 (73%), SMO (20%), and SUFU (8%). P53 is implicated in 61% of cases, along with other tumor-related genes such as MYCN (30%), PPP6C (15%), and STK19 (10%). Individuals working in sun-exposed environments face a higher risk of BCC compared to the general population (OR 1.43; 95% CI 1.23 - 1.66).<sup>7,8,9</sup>

**Squamous cell carcinoma (SCC)**

Sun exposure plays an important role in the pathogenesis of actinic keratosis (AK), a precancerous skin lesion, and squamous cell carcinoma. It is estimated that the risk of progression to cancer for AK is 0.025-20% per year.<sup>10</sup>



**Figure 3. Diagram of the pathogenesis of SCC. UVA and UVB both play a role in the pathogenesis of SCC 1**

UVB causes mutations that change C to T or CC to TT, accounting for the majority of mutations causing squamous cell carcinoma (SCC). UVA causes mutations through the generation of the main oxidant radicals, where OH<sup>-</sup> radicals cause G to T. These mutations on P53 result in a loss of function in controlling cell death and inhibiting apoptosis. P53 mutations account for 90% of ozone-related SCC and 75 - 80% of actinic keratosis (AK) cases.<sup>12</sup>

### Cutaneous melanoma

UV plays a role in the pathogenesis of melanoma in sun-exposed sites. Additionally, melanoma in covered areas, such as the soles of the feet, has a different pathogenesis. Epidemiological studies indicate that intermittent exposure to intense UV rays causing sunburn is associated with a higher risk of developing melanoma than prolonged cumulative exposure.

The pathogenesis is also through direct effects on DNA caused by UVB and the generation of free radicals caused by UVA, with the involved genes being P53 and CDKN2A. The presence of lentigo maligna lesions in the exposure area serves as evidence for the role of UV in melanoma pathogenesis.<sup>1</sup>

### 3. EVIDENCE THAT SUNSCREEN PREVENTS SKIN CANCER

Sunscreen consists of inorganic and organic substances that, when applied to the skin, reduce the intensity of ultraviolet rays and possibly visible light rays reaching the stratum corneum of the skin. Sunscreens are divided into two main groups according to their chemical properties: organic sunscreens and inorganic sunscreens. There are a total of 17 sunscreen active ingredients licensed in the US and 27 in Europe.<sup>13,14</sup>

FDA Monograph Sunscreen Ingredients	Amount of Ray Protection		Chemical (C) or Physical (P)
	UVA	UVB	
Aminobenzoic acid (PABA)	○	●	C
Avobenzene	●	◐	C
Cinoxate	◐	●	C
Dioxybenzone	◐	●	C
Ecamsule	●	◐	C
Homosalate	○	●	C
Menthyl anthranilate	◐	●	C
Octocrylene	◐	●	C
Octyl methoxycinnamate	◐	●	C
Octyl salicylate	○	●	C
Oxybenzone	◐	●	C
Padimate O	○	●	C
Phenylbenzimidazole	○	●	C
Sulisobenzene	◐	●	C
Titanium dioxide	◐	●	P
Trolamine salicylate	○	●	C
Zinc Oxide	●	●	P

Protection Level: ● = extensive ◐ = considerable ◑ = limited ○ = minimal

**Figure 4. Sunscreen active ingredients licensed in the US14**



When using sunscreen, we care about the effectiveness of sunscreen against both UVA and UVB. The effectiveness of sunscreens against UVA is expressed by the UVA protection factor (UVA-PF), and against UVB by the sun protection factor (SPF). A broad-spectrum sunscreen should have a critical wavelength of at least 370 nm and a UVA-PF rating of at least 1/3 of the SPF. (The critical wavelength is the wavelength at which the area-under-the-absorbance-curve represents 90% of the total area-under-the-curve in the UV region). In this way, broad-spectrum sunscreens block UVB and most UVA rays.<sup>15,16</sup>

Due to the long latent period of basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) from exposure to UV, the first studies on the efficacy of sunscreen on actinic keratosis (AK) prophylaxis were reported. Naylor and colleagues studied a group of 53 patients who applied SPF29 sunscreen for 2 years. The results showed that the group using sunscreen had less AK damage than the group that didn't apply it, which was statistically significant.

Green and colleagues conducted a prospective study on Australians using SPF17 sunscreen. The number of cases of squamous cell carcinoma (SCC) in the group that applied sunscreen was statistically significantly lower than that in the group that did not use sunscreen.

For melanoma, evaluating the effectiveness of this sunscreen in cancer prevention is often challenging to design studies and seems unethical. Therefore, to assess the effectiveness in preventing melanoma, researchers evaluate the appearance of moles in the study. Gallagher et al confirmed the effectiveness of sunscreen

in preventing the appearance of moles in 485 children aged 6-9 years using SPF30 sunscreen.

#### **4. WORLDWIDE RECOMMENDATION ON THE USE OF ANTI-SUN CREAM IN SKIN CANCER PROTECTION**

In the 2018 American Academy of Dermatology (AAD) SCC treatment guidelines, sun protection is recommended through physical shielding and the use of broad-spectrum sunscreen. The AAD's 2018 BCC Guideline made similar recommendations.<sup>20,21</sup>

##### **In children, the American Academy of Pediatrics recommends**

- For babies younger than 6 months: Use sunscreen on small areas of the body, such as the face, if protective clothing and shade are not available.

- For babies older than 6 months and children: Apply to all areas of the body, but be careful around the eyes. If the baby rubs sunscreen into the eyes, wipe their eyes and hands clean with a damp cloth. If the sunscreen irritates their skin, try a different brand or sunscreen with titanium dioxide or zinc oxide.

- Apply 15 - 30 min before going outside. Reapply every 2 h and after swimming, sweating, or drying off with a towel.

- Use a sunscreen that says "broad-spectrum" on the label. Avoiding those that contain oxybenzone.

- Use a broad-spectrum sunscreen with a sun protection factor (SPF) of at least 15 (up to SPF 50).

- Supplementation with vitamin D 400 IU daily for children age < 1 year, 600 IU for children age >1 year.

### For adults, the American Dermatology Association's recommendation

- The recommended amount of sunscreen in order to evenly coat the skin, consider its irregularities, is 2 mg/cm<sup>2</sup>.

- Apply broad-spectrum sunscreen with SPF30. Sunscreens without intangible filters (titanium dioxide and zinc oxide) are generally better accepted by people of color because of their better cosmesis on dark skin.

- Apply sunscreen to dry skin 15 - 30 min before going outdoors. When outdoors, reapply every 2 h to all exposed skin, and after perspiring or swimming.

- Take vitamin D supplement: 600 IU daily age 1 - 70 year, and 800 IU daily age > 70 year for subjects at risk of vitamin D deficiency or using sun protection measures vigorously.

### 5. CONCLUSION

Besides using sun protection methods such as shading, sunscreen plays an important role in preventing skin cancer. When using sunscreen, be aware of the product's SPF and UVA-PF. In addition, it is necessary to follow the recommendations on application time, application dosage, and vitamin D supplementation for individuals at risk of vitamin D deficiency or using excessive sun protection methods.

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