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**RESEARCH ARTICLE**

# Exposure to solar ultraviolet radiation is the major cause of most skin cancers

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## *Abstract*

Overexposure to UVR can lead to sun burn, immunological changes, precipitation or exacerbation of photosensitivity, accelerated skin aging, and skin cancer. An association between sunlight and skin cancer was first noted in the late 1800's when the increased cancer susceptibility of fair skinned individuals exposed to a large amount of sunlight was documented. The incidence of skin cancer has been increasing rapidly in recent years, and this has been attributed to depletion of the ozone layer and an increased frequency of recreational activities involving exposure to the solar rays. Exposure to UV light is considered to be a major risk factor for the development of squamous cell carcinoma (SCC), basal cell carcinoma (BCC), and melanoma. Alterations in the p53 tumor suppressor gene have been detected at a relatively high frequency in human skin tumors (=50% for SCC and BCC). The base changes observed inp53 from these tumors are similar to those induced in model systems by UV light, implying that this agent is responsible for the mutations. One of the cellular targets for sunlight induced damage is DNA.



## INTRODUCTION

**description**Overexposure to UVR can lead to sun burn, immunological changes, precipitation or exacerbation of photosensitivity, accelerated skin aging, and skin cancer[(1)]. An association between sunlight and skin cancer was first noted in the late 1800's when the increased cancer susceptibility of fair skinned individuals exposed to a large amount of sunlight was documented [(2)].Wavelengths in the UV-A (320-400 nm) and UV-B (280-320 nm) regions of the solar spectrum are thought to be responsible for the carcinogenicity because they are able to penetrate the ozone layer and reach the earth. The incidence of skin cancer has been increasing rapidly in recent years, and this has been attributed to depletion of the ozone layer (which normally blocks shorter wavelength UV-C (190-280 nm) light) and an increased frequency of recreational activities involving exposure to the sun [(3)].Exposure to UV light is considered to be a major risk factor for the development of squamous cell carcinoma (SCC), basal cell carcinoma (BCC), and melanoma. The cellular origins of SCC and BCC are epithelial keratinocytes, whereas melanoma originates from melanocytes present in the epithelium. The role of sunlight in the development of melanoma is more controversial than that for SCC or BCC [(4)]. Exposure to UVR is the main cause of melanoma and NMSC. [(5)] UVR induces skin cancer by three mechanisms; direct DNA damage leading to mutation; production of activated oxygen molecules that in turn damage DNA and other cellular structures; and localized immunosuppressant blocking the body's natural anticancer defenses [(6, 7)] The UVR wavelengths primarily responsible for skin cancers are in the UVB (280 to 320 nm) and UVA (320 to 400 nm) range. Early research focused on UVB, in the belief that this component of natural light was more important in carcinogenesis. [(8)] Recent work recognizes the role of UVA as well. [(9)] UVA reaches melanocyte far more than UVB. It should be noted that UVA penetrates more deeply than UVB (Fig-2), SO the cellular and DNA damages may be expected in deeper skin layers**. On**average, the epidermal layers overlying the basal layer in Caucasian skin absorb 56% of the UVB and only 27% of UVA (Fig-2). [(10)] As UVB is absorbed in the epidermis by various molecules such

as the keratins and DNA, it can suppress immune reaction, induce tolerance to antigens, up regulate gene expression, and induce mutations. [6] UVB directly mutates DNA. **In TP53 tumor suppressor gene functioning**; DNA damage induces P53 expression. In turn, p53 induces expression of p21, which prevents progression of the cell cycle from G1 to S Phase by inhibiting CDK2 and CDK4. Cell cycle blockade permits repair of DNA before replication in S phase to prevent retention of acquired mutations. If DNA damage is severe, cell undergo programmed cell death mediated by p53-induced BAX. This in turn, leads to programmed cell death as BAX binds to BCL-2 and inhibits its anti-apoptotic activity. In addition, p53 induces expression of HDM-2, which, in turn, down regulates p53 to permit cell cycle progression when appropriate. $P14^{ARF}$ inhibits HDM-2 to promote stabilization of P53(Fig-1). **Inactivation of the TP53 gene** would eliminate P53-induced cell cycle blockade and the cell death response to sever DNA damage, thus preventing mutations from being repaired and allowing them to accumulate. However, when P53 is inactivated, blockade of cell cycle progression would not occur in response to DNA damage. This would prevent repair of mutations prior to DNA replication and facilitate their retention in genomic DNA. Moreover, inactivation of P53 would prevent induction programmed cell death in response to sever DNA damage. Therefore, damaged cells that have acquired mutations would persist. Thus, the P53 gene, function as a **guardian of the genome**. [11, 12]This leads to either growth arrest and DNA repair or apoptosis. Apoptosis serve a protective role by eliminating cells with damaged DNA and malignant potential. The balance between survival and apoptogenic factors determines the final cell fate, and growing evidence suggests that the deregulation of this balance by chronic UVB stress, results in the development of skin malignancy. [13] However, UVB also plays an important role in stimulating **Photoprotective adaptation of the skin**. UVB-induced mutations (thymidine dinucleotide) in the epidermis are believed to stimulate a Photoprotective, which includes the synthesis and release of melanosomes by melanocyte. This in turn reduces the penetration of UVR to the basal epidermis and melanocyte. [14]. Photoprotective response also includes the proliferation of keratinocytes, leading to a thickening of the stratum corneum, improved scattering of UVR, and reduced UV penetration of the skin. [15,16]

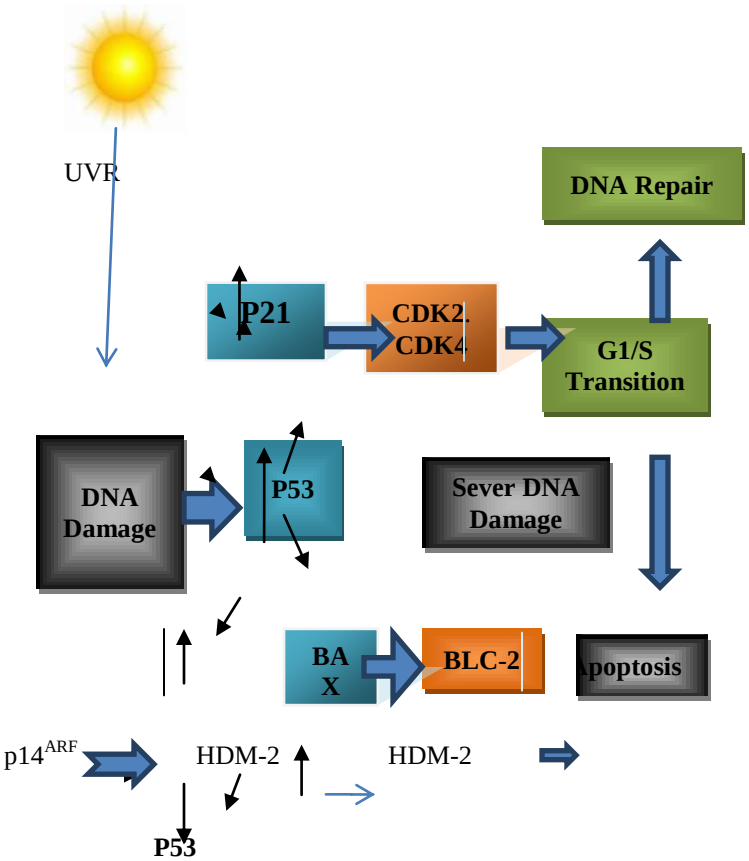


**Fig-1: DNA damage with sun rays exposures.**

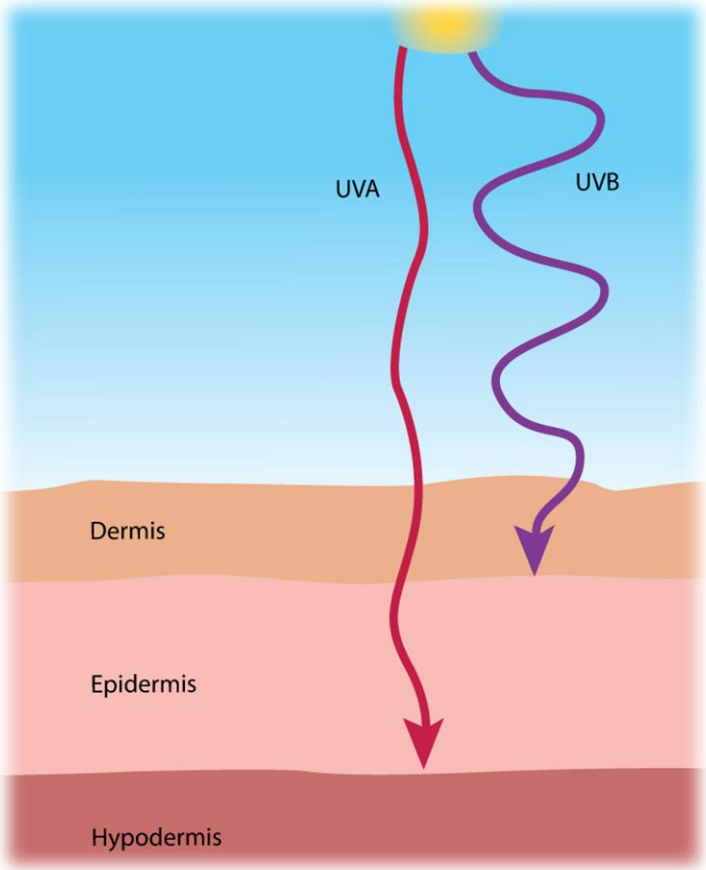


**Fig-2: penetration of UVB and UVA into skin.**

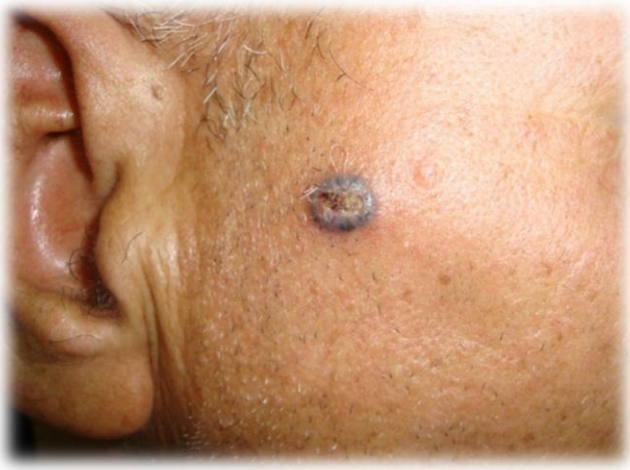

**Fig-: BCC due to sun exposures.**

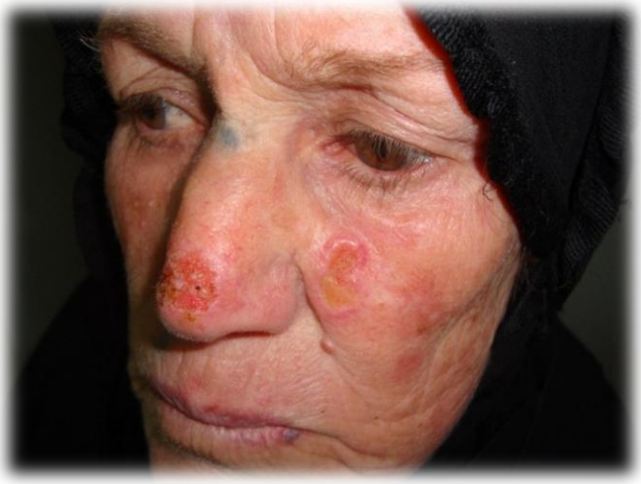

**Fig-: SCC due to sun exposures.**

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