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A REVIEW ON THE ROLE OF INFLAMMATION IN SKIN CANCER AND NEW TREATMENT APPROACHES

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ABSTRACT

The rate of skin cancer has escalated rapidly over the past decade, affecting both melanoma and non-melanoma types. Skin cancers primarily consist of keratinocyte cancers, including cutaneous squamous cell carcinoma, basal cell carcinoma, and melanoma. This review highlights recent progress in skin cancer treatments. In addition to chemotherapy, options such as immunotherapy, targeted therapy, and photodynamic therapy (PDT) are available for skin cancer. Furthermore, the combination of PDT with chemotherapy, radiation, immunotherapy, and surgery is currently being explored. This review will focus on the pathophysiology of skin cancer and existing therapies utilized in the topical treatment of skin cancers, as well as introduce novel treatments that may offer benefits for these conditions.

KEYWORDS: Skin cancer, Melanoma, Non-Melanoma skin cancer, Tumorigenesis, Inflammation, Inflammasomes, Immune cells, Treatment.

INTRODUCTION

Skin carcinoma is among the most lethal forms of cancer, first identified by Laennec (melanoma), Jacob (basal cell carcinoma), and Bowen (squamous cell carcinoma in situ) in 1804, 1827, and 1912, respectively. As of 2020, skin carcinoma ranks as the fifth most frequently diagnosed cancer globally. The skin is the largest organ of the human body, and it is composed of several layers. From the outside in, the skin apparatus consists of the epidermis, dermis, and hypodermis. The presence of neurovascular, glandular, mesenchymal,

and epithelial elements characterizes the first two strata.[1] The epidermis is composed of keratinocytes, which, during their differentiation, become corneocytes and form a barrier that protects the body from various physical, chemical, and immunological environmental agents. As a result, the epidermis is the most susceptible to exposure to environmental stressors such as UV radiation, ozone, and air pollution. Langerhans cells and resident T cells support cutaneous immune surveillance, and melanocytes in the basal epidermal layer create melanin, which provides UV protection. While the hypodermis binds the skin and insulates the body, the dermis offers structural support, suppleness, and contains blood vessels, nerves, and numerous immunological cells. Skin conditions like erythema, edema, dermatitis, psoriasis, photoaging, and cancer may develop as a result of a disruption in the function of the skin barrier.[1,4] The biggest organ in the body, the skin interacts with a variety of external elements to protect the organism from radiation, mechanical pressure, and viruses. UV radiation (UVA and UVB) from the sun is one of the primary environmental aggressors that causes several biological effects, including significant DNA damage and the production of reactive oxygen species (ROS). These changes have the potential to both lower inflammation and accelerate the development of tumors. Inflammasomes and other intracellular protein complexes can be activated by ROS and damaged DNA.[2] Skin cancer is a global epidemic and a diverse group of cancers. Over 90% of all skin cancers are these types. Skin cancer accounts for one in three cancer diagnoses globally, with NMSCs being the most prevalent type.[5]

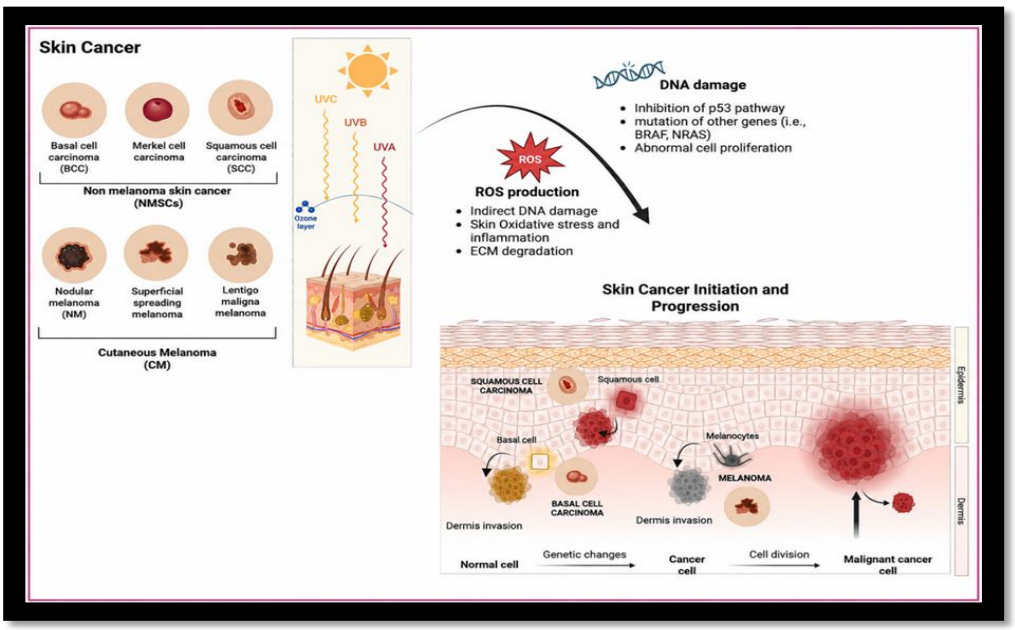


Figure No.: 1 Skin Cancer Initiation and Progression.

The two main categories of skin malignancies are melanoma skin cancer (MSC), which includes cutaneous melanoma (CM), and non-melanoma skin cancer (NMSC), which includes squamous cell carcinoma (SCC) and basal cell carcinoma (BCC). The bulk of skin cancer instances are non-melanoma skin cancers, namely BCC and SCC, with BCC accounting for about 80% of NMSC diagnoses. With an anticipated 1,234,533 cases identified worldwide, NMSC was the fifth most frequent cancer in the world, according to recent global data from GLOBOCAN (2022). With an expected 331,722 new occurrences, melanoma of the skin was the 17th most frequent malignancy at the time. It is noteworthy that due to increased UV exposure and the usage of treatment-based reporting rather than population-wide registries. Approximately 69,416 deaths were caused by NMSC. Conversely, melanoma is less prevalent but far more aggressive, accounting for about 58,667 fatalities globally. These numbers demonstrate how common skin cancer is throughout the world and how crucial early identification and treatment are. In order to lower morbidity and financial cost, early identification techniques—such as routine skin inspections using dermoscopy and reflectance confocal microscopy—and limiting exposure to risk factors—such as radiation, arsenic, and immunosuppressants—remain crucial.[3]

Skin structure and function

The skin is the largest and most dynamic organ of the body, making up 16 of the body weight, with a face area of 1.8 m2, and positioned at the interface between the body and terrain. Skin serves as the armor for the body against mechanical, thermal, and physical injury and dangerous substances. There are three structural layers of the skin: epidermis, dermis, and subcutaneous subcaste.[6] Epidermis is an external and continually regenerative, stratified epithelium devoid of blood or whim-whams inventories of roughly 5 – 100 μm consistence. It's composed of several distinct cell populations, keratinocytes and melanocytes being the main ingredients. keratinocytes, which comprise 95 of the epidermis, are arranged in four layers. The inner subcaste is the stratum germinativum (stratum basale, rudimentary subcaste), from which columnar- shaped keratinocytes divide to resettle to the coming subcaste. The stratum spinosum (spinous subcaste) is composed of polygonal keratinocytes that are ultimately more condensed. Further isolation of the cells leads to the stratum granulosum (grainy subcaste), which contains basophilic grains. In thick skin areas, such as the soles of the feet or the palms of hands, there's a clear subcaste of smoothed cells called the stratum lucidum. The remotest subcaste is the stratum corneum (wanton subcaste), which contains keratin and dead cells that confer to the skin its protective function.[8]

Types of skin cancer

There are four different types of skin cancer rudimentary cell melanoma (BCC) and scaled cell melanoma (SCC), inclusively appertained to as non-melanoma skin cancers (NMSC) or keratinocyte melanoma; carcinoma and other non-epithelial skin cancer. BCC and SCC regard for roughly 80 and 16 of all NMSC, independently. cell types, causes, and threat factors associated with skin cancer. Melanoma accounts for only 10 of skin cancer cases, but it's the most serious type, which can also do in other body organs. Along with carcinoma and keratinocyte cancers, there are some other less common types of skin cancer, e.g., Merkel cell melanoma, Kaposi's sarcoma, cutaneous (skin) carcinoma, skin adnexal excrescences, dermatofibrosarcoma protuberans, and angiosarcoma.[9]

Non-Melanoma Skin Cancer

The primary cells of the epidermis are keratinocytes, whose unchecked growth may cause NMSCs. New treatment targets or inflammatory markers for prognosis and diagnosis may be revealed by the inflammatory pattern linked to carcinogenesis.[9,10] 50 proteins associated with keratinocytes were found through proteome profiling; these included proteins related to the immune system (e.g., α-2 macroglobulin-like protein-1, α-2 macroglobulin-like protein 2, and IFN regulatory factor-6 (IRF-6)), differentiation (e.g., dermokine and calmodulin-like protein 5), and motility (e.g., integrin ß4).[13] However, as the aforementioned proteins are highly influenced by the inflammatory state, it was discovered that integrin 4 and α-2 macroglobulin-like protein-1 were decreased when keratinocytes were stimulated with IL-1. The NF-kB pathway, which is heavily implicated in angiogenic and pro-tumorigenic processes, was stimulated by IL-1. All of these changes were also discovered to support the connection between inflammation and carcinogenesis in epidermoid carcinoma cells.[11,12]

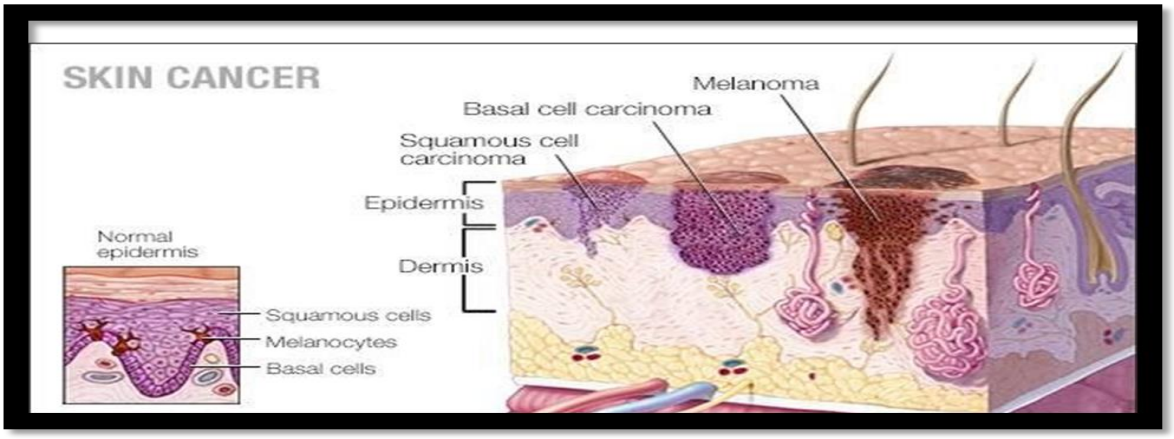


Figure No.: 2 Skin Cancer.

Squamous Cell Carcinoma

The risk of developing cSCC is six times higher in patients with a history of psoralen and UVA (PUVA) exposure for psoriasis. Chronic or nonhealing wounds produce chronic inflammation, which is linked to the development of cSCC. The pathophysiology of cSCC frequently involves mutations; the rate of mutations in these lesions is four times higher than that of melanoma skin cancers. A C to T signal-base transitional mutation on the dipyrimidine sites of tumor protein 53 (TP53) is the most frequent mutation linked to cSCC; Further mutations have been observed at the Notch homolog 1 tumor suppressor, Ras proteins, and cyclin-dependent kinase inhibitor 2A (CDKN2A).[8,9]

Squamous cell carcinoma is a secondary form of skin cancer, accounting for 99% of all NMSC patients. It develops in the keratinocyte cells of the outer layer of the epidermis and appears as scaly patches or red, firm bumps.[25] This type of cancer is mainly caused by overexposure to UV rays and is more common in light-skinned people. Several factors contribute to the risk of SCC, including a light complexion, aging, burn scars, chronic skin ulcers, immune suppression, chemical carcinogens, and primarily UV radiation.[22] The development of CSCC has been connected to a number of molecular mechanisms. UV-induced instability is one of the early events in CSAA. There may be therapeutic implications because CSCC has the highest mutational burden of any solid tumor. Next are suppressor genes like CDKN2A and NOTCH, as well as oncogens like RAS.[24, 26]

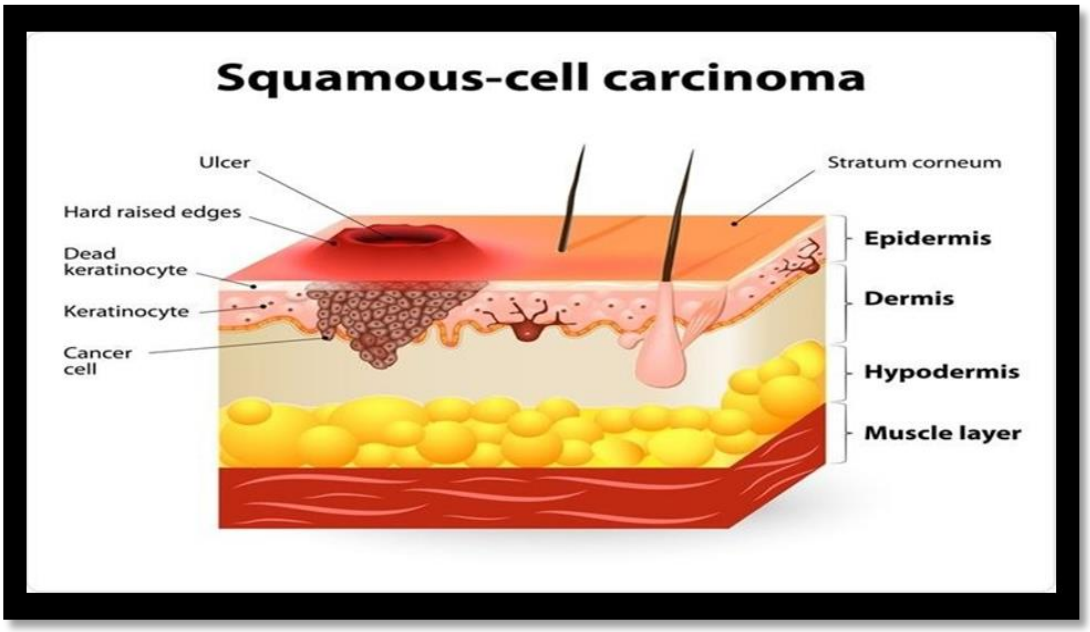


Figure No.: 3 Squamous-cell Carcinoma.

Basal Cell Carcinoma

BCCs represent slowly developing keratinocyte carcinomas that scientists believe originate from hair follicle stem cells. This form of cancer stands as the most prevalent malignancy globally, affecting approximately 5% of Caucasian individuals. Global occurrence rates have risen over the past twenty years, though this growth has stabilized in certain areas due to enhanced cancer detection programs and better sun protection awareness.[14]

BCC development occurs more frequently in people with pale complexions, bright-colored eyes, poor tanning ability, and tendency toward freckle formation. Furthermore, individuals with compromised immune systems show elevated BCC rates. While most BCCs develop randomly through UV-triggered genetic changes, several hereditary conditions also contribute to their formation. Nevoid basal cell carcinoma syndrome (Gorlin syndrome) represents an inherited disorder affecting 1 in 40,000 to 57,000 individuals in the general population. This condition involves abnormal activation of hedgehog (Hh) pathway messaging, leading to numerous BCCs, particularly the infundibulocystic type. This pathway controls skin formation and manages cell growth and specialization in hair follicles and oil glands.[16,18]

Regarding environmental influences on BCC development, excessive solar UV radiation stands as the primary external risk factor, creating an exceptionally high tumor mutation load (TMB). Using tanning beds, especially during youth, correlates with a 40% increased chance of BCC formation. In the United States, indoor tanning accounts for 3.7% of BCC cases.[18] Additionally, medications that increase light sensitivity, including tretinoin and specific antibiotics, have been linked to higher BCC risk. Previous exposure to ionizing radiation also contributes to BCC formation; research involving 1,690 patients who underwent radiation treatment showed a 2.3 times greater relative risk for BCC development, with this risk growing among those who received radiation during younger years. Finally, having previously developed BCC creates risk for additional lesions, with three-year cumulative risk reaching as high as 44% in patients with prior BCC history.[20,21]

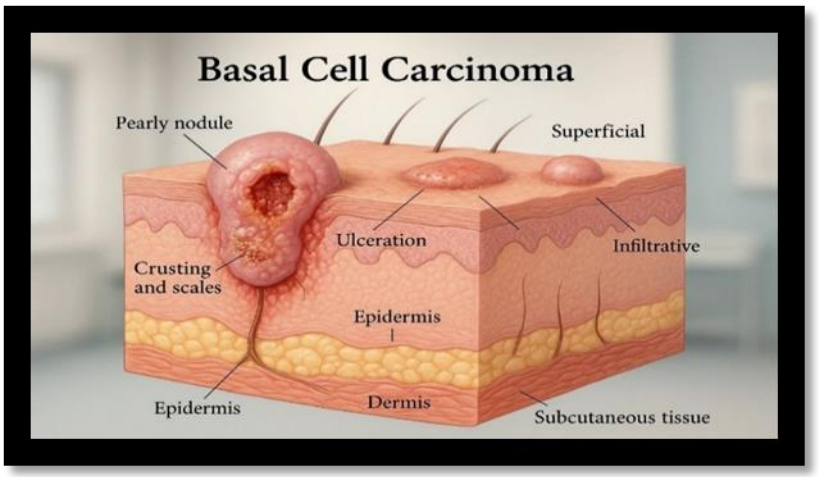


Figure No.: 4 Basal cell Carcinoma.

Merkel Cell Carcinoma

MCC is a rare and aggressive type of cutaneous neuroendocrine cancer, characterized by a poor prognosis and a high likelihood of local recurrence, with a 5-year recurrence rate reaching up to 40%, as well as potential for distant or lymph node metastasis.[8] It usually occurs in older individuals, especially at skin sites with high UV exposure, such as the head and neck. Currently, around 3000 new MCC cases are diagnosed each year. Multiple studies, including a recent comprehensive review by Mohsen and colleagues, indicate that MCC incidence is increasing significantly and is expected to exceed 5,000 cases annually by 2030, likely due to the aging population.[16,19]

Although the exact pathogenesis remains under investigation, two main causes of MCC are recognized. Most MCC cases result from the integration of the Merkel cell polyomavirus (MCPyV), first identified in 2008. The remaining 20% to 40% of cases show high tumor mutational burden (TMB), typically caused by UV-induced mutagenesis that often inactivates TP53 and RB1.[20] Only about 4% of MCC patients are younger than 50, and genetic risk factors for early-onset MCC include variants linked to hereditary cancer syndromes, such as ATM, BRCA1/2, TP53, and MAGT1.[22]

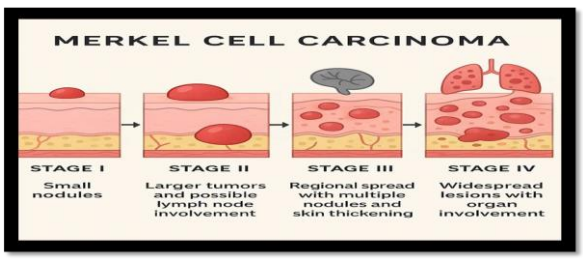


Figure No.: 5 Merkel cell Carcinoma.

Melanoma skin cancer

Melanoma is an aggressive malignant tumor originating from melanocytes, which reside in the basal layer of the epidermis. The development of melanoma involves the accumulation of genetic alterations that activate oncogenes, deactivate tumor suppressor genes, and impair DNA repair, especially when exposed to ultraviolet radiation. These changes can lead to uncontrolled growth of melanocytes and ultimately cause malignancy.[29] In 2007, about 70,000 people in the US were diagnosed with malignant melanoma. Most of them were cured, but approximately 1000 people still die each year from melanoma skin cancer. Notably, 75% of skin cancer-related deaths were due to malignant melanoma alone.[30] To detect melanoma clinically, we can use the ABCD rule, which involves first, asymmetry—where one side of the lesion doesn't match the other. Second, border irregularity—edges of melanoma-affected skin are uneven or poorly defined. Third, color variation—melanomas often display multiple colors such as brown, black, tan, blue, or red. Finally, diameter—the size of the lesion is typically larger than 6mm.[32,33]

The four main subtypes of invasive cutaneous melanoma are categorized as follows: [30 to 34]

- Superficial melanoma: These are the most common subtype, representing about 75% of melanomas. They appear as mole—like pigmented skin lesions that have changed in size, shape, or color. In women, they are typically found on the legs, while in men, on the trunk.
- Nodular melanoma: accounts for approximately 15-30% of melanoma cases. Since it does not have a radial growth phase, it tends to expand more quickly in depth than in width. Older individuals are more prone to developing nodular melanomas on their heads and necks.
- Legtigo malin: It is the second most common melanoma subtype. It typically appears as a small, flat, tan lesion with irregular borders on sun-exposed skin. Over time, the spot enlarges and changes color. These melanomas are much more common in adults over 60 and are often called “senile freckles.”
- Acral lentiginous melanoma: It is a rare subtype, accounting for about 2 to 3% of all melanoma cases, making it the least common type. It typically appears on the soles, toes, palms, fingers, and nail beds. Unlike other melanoma types, it is not associated with sun exposure.

Inflammation in skin cancer

Many non-immune cells are included in the picture of inflammation. Numerous chemicals can stimulate keratinocytes, the skin's main cellular component. When stimulated, these cells release pro-inflammatory cytokines that control both innate and adaptive immunity. Together with a lower number of melanocytes and skin-resident DCs (LCs), keratinocytes release immune-related substances (such as growth factors and cytokines) that create an inflammatory local environment and encourage the development of cancer. T cells can be activated by keratinocytes in two separate ways. Thus, granulocyte-macrophage colony-stimulating factor (GM-CSF), tumor necrosis factor (TNF)-α, IL-6, IL-7, IL-12, IL-15, and IL-18 can all be released to increase T cell activity. IL-1Rα, IL-10, α-melanocyte-stimulating hormone (α-MSH), chemokine (C-X-C motif) ligand 10 (CXCL 10), counter-IL-1, and prostaglandin E2 (PGE2) generated by keratinocytes can all inhibit T cell activity. Conversely, T cells can release IFN-α, IL-17, and IL-4, which affect the activities of keratinocytes.[2]

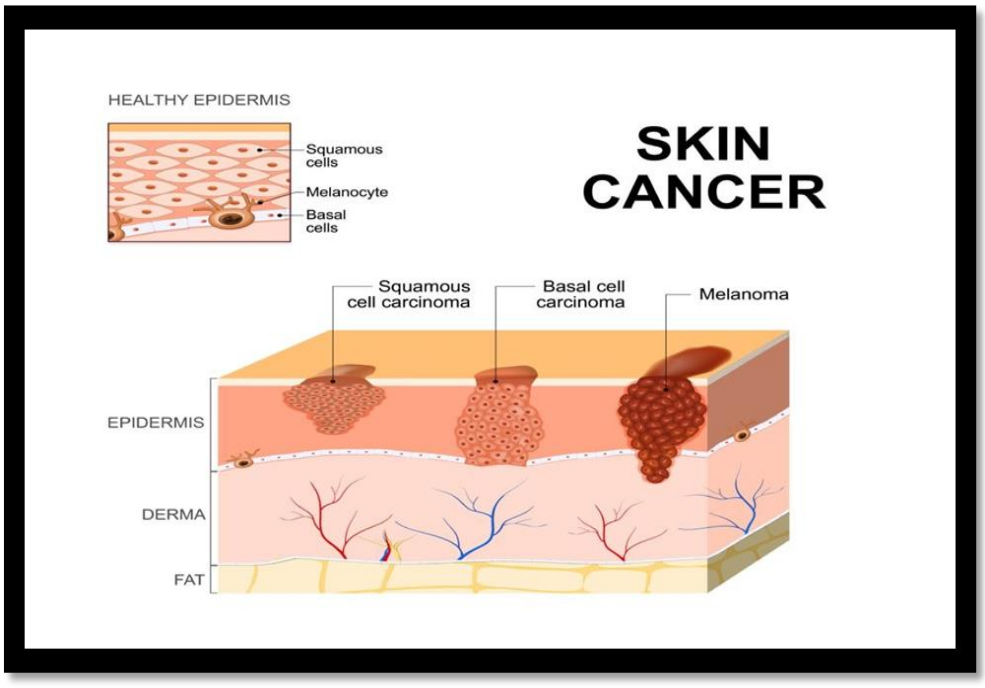


Figure No.: 6 Skin Cancer.

UV-induced DNA damage is known to be the main cause of skin carcinoma, and it also contributes to oxidative stress, DNA damage, carcinogenesis, and photoaging in melanoma and NMSC (SCC, BCC). The three types of UV radiation (UVR) include UVA (320-400 nm: UVA2 320-340 nm, UVA1 340-400 nm), UVB (290-320 nm), and UVC (180-290 nm).

Because the atmospheric ozone (O3) layer absorbs UVC and partially filters UVB, 90–95% of UV that reaches the Earth's surface is UVA, 5–10% is UVB, and 80% is UVA1, which can pass through the deep dermal layer. Due to UV-catalyzed photolytic dissociation, which depletes ozone and is associated with an increase in skin cancer and dermatological conditions, emissions of chlorofluorocarbons (CFCs) have contributed to ozone depletion in recent decades.[1]

Inflammasomes are produced by pro-caspase-1, an adaptor known as apoptosis-associated speck-like protein (ASC), and a cytoplasmic sensor. This large family is defined by inflammasome sensors, including pyrin, NOD-like receptor with pyrin (NLRP)1, NLRP3, and NOD-like receptor with caspase recruitment domain (NLRC)4.[6]

When UV radiation hits the skin, squalene in sebaceous lipids oxidizes, causing inflammatory reactions and acting as a danger signal that activates inflammasomes. Human BCC exhibits higher amounts of IL-1ß, caspase-1 activation, and NLRP3, the most prevalent kind of inflammasome, than normal skin.[8] Pannexin-1 channels involved in keratinocyte differentiation that can induce inflammasome activation were also identified in melanoma progression. NLRP1 is strongly expressed in human skin as compared to other NLRs.[7] At the genetic level, polymorphisms detected in NLRP1/NLRP3 and in inflammasome-related genes [e.g., caspase recruitment domain (CARD)8, IL-1ß and IL-1] were found to be associated with skin melanoma, related to both susceptibility and progression.[4] Inflammasome involvement was found to be correlated with melanoma stages. Consequently, auto-inflammatory characteristics, such as gain-of-function mutations in NLRP3, are present in cells isolated from late-stage human melanomas, and they spontaneously release IL-1ß without stimulation. This study has shown a strong relationship between IL-1 constitutive secretion and melanoma aggressiveness. The ASC component of the inflammasome promotes to melanoma tumorigenesis while inhibiting cancer cells linked to the relationship between inflammation and carcinogenesis in primary melanoma.[9] ASC has a tumor-suppressive function in keratinocytes, while it is pro-tumorigenic in myeloid cells. Collectively, new knowledge suggests that among all NLRPs, NLRP1 is the predominant inflammasome sensor in human skin. In skin models, cytokine stimulation with IL-1α, IL-1ß, and IL-18 has been shown to induce epidermal hyperplasias, an adjacent characteristic of tumor tissue.[10,11]

Role of inflammation in skin cancer

The color that determines skin and hair color. They're located in the rudimentary subcaste of the epidermis, which comprise from 5 to 10 of the cells and in hair follicles, and are also set up in other anatomical areas similar as the inner observance, the eye, and the meninges.[15]

Dermis, the middle subcaste of the skin set up below the epidermis, is composed of a tough, probative cell matrix. The dermis contains fibroblasts, which produce collagen, elastin, and structural proteoglycans, together with vulnerable-competent mast cells and macrophages. Collagen filaments, which make up 70 of the dermis, give skin its strength, pliancy, and durability. Dermis contains hair follicles, sweat glands, blood vessels, and jitters that are held in place by collagen Subcutis or subcutaneous subcaste consists of loose connective tissue and fat. It helps the body conserve heat and has a shock- absorbing effect that helps protect the body's organs from injury.[18]

Skin has several functions, the most important being to form a physical hedge to the terrain, allowing and limiting the inward and outward passage of water, electrolytes, and colorful substances while furnishing protection against microorganisms, ultraviolet radiation (UVR), poisonous agents, and mechanical cuts. Its other functions are sequestration, temperature regulation, sensation, and conflation of vitamin D and the protection of vitamin B folates.[20]

New treatment approaches

Early diagnosis and prompt treatment are essential for better outcomes in any skin cancer. As one of the most prevalent cancers globally, representing over a third of all cancer cases, timely detection is vital. Delays can allow the disease to progress, raising the risk of metastasis and decreasing the likelihood of successful treatment.[27]

Surgical resection is highly effective in most cases, but the decision to proceed depends on factors like the patient's comorbidities, the tissue involved, and the likelihood of resistance to repeated treatments. Patient preferences, including convenience, costs, and tolerance, are also taken into account.[25]

Topical Treatment

Imiquimod 5% cream (ALDARA®) has FDA approval for treating non-facial superficial BCC. Multiple studies show that applying imiquimod twice daily for 6-12 weeks can completely cure superficial BCC. Sometimes, treatment frequency is increased from 3 to 7

times per week and then adjusted to once or twice daily based on skin tolerance to manage mild to moderate irritation. Patients can control skin irritation levels by modifying how often they apply the cream.[20,22]

In a trial with 601 patients undergoing histological confirmation of superficial BCC, topical imiquimod cream (applied once daily, five times a week for six weeks) was shown to be more effective than methylaminolevulinate photodynamic therapy.

Tazarotene, a selective acetylcholine retinoid (Tazorac®), may be used safely for treating minor BCCs. It is believed to work by inhibiting cell growth and promoting differentiation in BCC cells, leading to regression of this type of skin cancer. Most resistant tumors showed keratotic differentiation. In one case series, 70.8% of BCCs decreased by more than 50% both clinically and dermoscopically, and 30.5% were cured without recurrence after three years.[27,44]

Excisional Surgery

Excisional surgery is a common approach for treating skin cancer. This method involves cutting the tumor in slices 1.5 to 2 mm deep for histopathological examination. Its primary benefit is resulting in a minimal scar. The main limitations include risks of infection, seroma, hematoma, and wound formation.[27]

Mohs micrographic surgery

Mohs micrographic surgery is a state-of-the-art technique for removing tumors under local anesthesia, allowing for the visualization and excision of the maximum tumor while minimizing damage to normal tissue. It is more cost-effective than traditional surgery and helps prevent the recurrence of BCC or SCC.[28,43]

Curettage and electrodessication

Curettage and electrodessication, also known as curettage and desiccation, is a specialized technique that destroys the cancerous lesion and surrounding normal tissues through cauterization and scraping with a curette. It is suitable only for small skin tumors and is not recommended for larger or high-risk tumors. As a result, it is the least preferred method.[27-28]

Cryotherapy

Cryotherapy is a treatment method that uses liquid nitrogen to freeze small BCC or SCC lesions until they are destroyed. Its primary benefit is that it typically avoids complications

like bleeding or scarring, while also achieving a high rate of tumor removal. However, this technique is rarely used for skin cancer treatment.[29]

Radiation therapy/radiotherapy

Radiation therapy, or radiotherapy, is an effective option for treating older patients with extensive or recurrent skin cancer who cannot withstand surgery or when tumor removal isn't surgically feasible.[30] This treatment mainly falls into three categories: conventional external radiation therapy, superficial x-ray therapy, and brachytherapy.[41] A less invasive technique, volumetric arc therapy, offers complex dose distribution and reduces damage to normal tissues.[32] However, its high cost, multiple visits required for treatment, and the potential for growth of aggressive phenotypes in some recurring tumors are notable limitations.[35]

Photodynamic therapy

Photodynamic therapy (PDT) is a unique non-invasive method that uses photosensitizers and lasers to destroy skin cancer cells. Photosensitizers are administered to target the tumor area, then activated by laser irradiation to produce singlet oxygen and other reactive oxygen species, which ultimately destroy tumor cells. Commonly used photosensitizers include hematoporphyrin derivative. However, a limitation of this technique is its high cost and reduced effectiveness against deep-seated tumors.

Immunotherapy, targeted therapy, and chemotherapy

Immunotherapy, targeted therapy, and chemotherapy are among the most promising adjuvant treatments for BCC, SCC, and melanoma. Whether combined with surgery, radiation therapy, or PDT, these therapies are strongly recommended as alternative options for effectively curing advanced skin cancer and preventing recurrence. They have also been shown to improve surgical outcomes for skin cancer patients. However, issues such as high costs and low patient compliance associated with immunotherapy and targeted therapy pose challenges.[38,39,40] Consequently, many patients turn to chemotherapy. Therefore, developing advanced treatment strategies to address these limitations is crucial for ensuring better patient adherence and improving outcomes.[36,37]

Inhibitors of Inflammation for the Prevention and Treatment of Skin Cancer

Substantiation suggests that inflammation is causally linked to carcinogenesis. COX- 2, the rate- limiting enzyme in arachidonic acid metabolism leading to PG conformation, is over-regulated in murine and mortal NMSC. Inhibition of COX- 2 by biochemical impediments or

inheritable omission decreases chemical- or UV-induced skin excrescence development. A number of beast models have shown that inhibition of COX- 2 helps skin cancer, including UVR- convinced skin carcinogenesis and two-stage skin carcinogenesis model in mice.[44]

Non-steroidal Anti-inflammatory Drugs (NSAIDs)

Medicines of this class include celecoxib, diclofenac, indomethacin, sulindac, aspirin, and ibuprofen. They act by repressing prostaglandin biosynthesis through the inhibition of COX. The expression of COX- 2 is linked to inordinate activation of intracellular signal transduction pathways comprising pro- line- directed serine/ threonine kinases and their downstream recap factors.[38]

Celecoxib, a COX-2 inhibitor, decreases macrophage and neutrophil infiltration into skin excrescences, as well as inflammation induced by 50 Gy radiation. Celecoxib at the boluses, determined to be original to doubly- diurnal boluses in humans, was effective at adding excrescence quiescence and diminishing multifariousness in furless mice exposed to UVR. This study showed a drop in PG conflation in the epidermis, as well as a statistically significant drop in excrescence yield.[44]

Diclofenac, a non-selective NSAID, is widely used to treat AK. In a study of 32 organ transplant donors with 3 or more AK lesions, those randomized to twice-daily treatment with 3% diclofenac showed a reduction in lesions, and no cases in the diclofenac group developed SCC in the treated areas. Therefore, diclofenac may help prevent the malignant transformation of AK.[38-40]

Naturally Occurring Plant Products

Dietary polyphenols, which are widely present in fruits, vegetables, dry legumes, and beverages (such as tea, coffee, juice, wine, beer) have gained considerable attention for the prevention of UV-induced skin photodamage, including the risk of skin cancer.[38]

Oral administration of green tea polyphenols (GTPs) to SKH- 1 furless mice resulted in significant inhibition of UVR-induced cutaneous edema, erythema, and bifold skin consistency (a biomarker of inflammation). Administration of GTPs in drinking water dropped COX- 2, PGE2, PCNA, and cyclin D1 and also significantly reduced the levels of pro-inflammatory cytokines in chronically UVB-exposed skin/ skin excrescences of mice. Topical operation of EGCG, an active element of green tea, in mice and humans, redounded

in the inhibition of UVB-induced products of PG metabolites (PGE2, PGF2- α, and PGD2), which play a critical part in inflammatory diseases, free radical generation, proliferative skin conditions, and skin excrescence creation.

Topical application of euphol insulated from the roots of Euphorbia kansui, markedly inhibited TPA- convinced observance edema and skin inflammation in DMBA/ TPA- treated manly CD 1 mice.[44]

CONCLUSION

Melanoma and non-melanoma skin cancers are among the most common cancers in mortality. Epidemiological and experimental substantiation suggests “habitual inflammation” to be one of the emblems in solar UVR and several other environmental agent-mediated skin cancers. The identification of recap factors, i.e., NF- κB, STAT3, and HIF- 1α, and their gene products, i.e., COX- 2, cytokines, chemokines, and chemokine receptors, suggests a critical part of inflammation in skin carcinogenesis. Considering the inflammatory component of the inauguration and its major, as well as satisfying, roles in creation, progression, as well as excrescence angiogenesis and metastasis, seditious pathways may become seductive targets for skin cancer prevention. Studies to help or minimize the exposure to given skin carcinogens and ongoing studies on assessing the role of colorful proinflammatory intercessors in carcinogenesis and assessing them as implicit targets for chemoprevention of skin cancers need to be enhanced/ encourage.

REFERENCES

1. Cortesi R, Sguizzato M, Ferrara F. Treatment of skin cancer: From conventional to nanotechnological approaches. *Biochim Biophys Acta Rev Cancer*, 2026; 1881(3): 189583. doi:10.1016/j.bbcan.2026.189583. [HYPERLINK "https: //pubmed.ncbi.nlm.nih.gov/41936875/?utm_source=chatgpt.com" PubMed Article Link]
2. Neagu M, Constantin C, Caruntu C, Zurac S. Inflammation: A key process in skin tumorigenesis (Review). *Oncol Lett*, 2019; 17(5): 4068-4084. doi:10.3892/ol.2018.9735.
3. Pareek A, Gupta R, Agrawal P, Jain V, Wadhwa L, Rathore M. Cannabinoids and skin cancer: Mechanistic insights, therapeutic potential, and translational perspectives. *Eur J Pharmacol*, 2026; 961: 176579. doi:10.1016/j.ejphar.2025.176579.
4. Castellsagué X, Díaz M, de Sanjosé S, Muñoz N, Bosch FX. Skin cancer: Epidemiology, disease burden, pathophysiology, diagnosis, and therapeutic approaches. In: Ward WH,

Farma JM, editors. *Cutaneous Melanoma: Etiology and Therapy*. Brisbane (AU): Codon Publications, 2017; 1-26.

5. Roky AH, Islam MM, Ahasan AMF, Mostaq MS, Mahmud MZ, Amin MN, et al. Overview of skin cancer types and prevalence rates across continents. *Cancer Pathog Ther*, 2025; 3(2): 89-100. doi:10.1016/j.cpt.2024.08.002. (HYPERLINK "https: //pubmed.ncbi.nlm.nih.gov/40182119/?utm_source=chatgpt.com" \o "Overview of skin cancer types and prevalence rates across continents - PubMed" pubmed.ncbi.nlm.nih.gov)
6. Caraviello C, Nunes GN, Teixeira GF, Bonamigo ND, de Moraes EP, Vilela PB, et al. Melanoma skin cancer: A comprehensive review of current knowledge. *Cancers (Basel)*, 2025; 17(2): 315. doi:10.3390/cancers17020315.
7. Jadhav LA, Mane SK. Nanocarriers in skin cancer treatment: Emerging drug delivery approaches and innovations. *J Drug Deliv Sci Technol*, 2024 Dec; 95: 105708. doi:10.1016/j.jddst.2024.105708. [HYPERLINK "https: //www.researchgate.net/publication/387156020_Nanocarriers_in_Skin_Cancer_Treatment_Emerging_Drug_Delivery_Approaches_and_Innovations?utm_source=chatgpt.com" Nanocarriers in Skin Cancer Treatment: Emerging Drug Delivery Approaches and Innovations]
8. Dugan MM, Asgari MM, Bichakjian CK, Karia PS, Torres JS, Martinez JC, et al. Current management of nonmelanoma skin cancers. *Dermatol Clin*, 2025; 43(1): 1-18. doi:10.1016/j.det.2024.08.001.
9. Daugaard ND, Johansen RT, Jensen RT, Schmidt M, Bønnelykke-Behrndtz ML, Fink T, et al. Characterization of human melanoma skin cancer models: A step towards model-based melanoma research. *Exp Dermatol*, 2024 Nov; 33(11): e15123. doi:10.1111/exd.15123.
10. Ibrahim AT, Ahmed MA, Abdullahi FD, Danjuma KM, Musa TM, McIver HH. Categorical classification of skin cancer using a weighted ensemble of transfer learning with test time augmentation. *Comput Biol Med*, 2024 Nov; 183: 109378. doi:10.1016/j.compbiomed.2024.109378.
11. Roky AH, Islam MM, Ahasan AMF, Mostaq MS, Mahmud MZ, Amin MN, et al. Overview of skin cancer types and prevalence rates across continents. *Cancer Pathog Ther*, 2025; 3(2): 89-100. doi:10.1016/j.cpt.2024.08.002.
12. Xie Y, Liu F, Li W, Yang Z, Yu J, Qin W, Zhang D, Kong L. Inflammation in cancer: Therapeutic opportunities from new insights. *J Hematol Oncol*, 2025; 18(1): 42. doi:10.1186/s13045-025-01625-7.

13. Omiyale O, Aremu AO, Okorie OD, Dada CG, George O. Inflammation and cancer: The most recent findings. *J Health Sci Med Res*, 2025; 43(2): 145-156. doi:10.31584/jhsmr.2025123.[HYPERLINK "http: //dx.doi.org/10.31584/jhsmr.20241082" http: //dx.doi.org/10.31584/jhsmr.20241082]
14. Andoh A, Nii AN. The role of inflammation in cancer: Mechanisms of tumor initiation, progression, and metastasis. *Cancers (Basel)*, 2025 Mar; 17(5): 812. doi:10.3390/cancers17050812.
15. Ekiner SA, Gül ES. Natural compounds modulating redox metabolism and inflammation: New insights in skin cancer prevention and therapy. *Free Radic Biol Med*, 2025 Nov; 231: 120-138. doi:10.1016/j.freeradbiomed.2025.08.015.
16. Ibrahim AT, Ahmed MA, Abdullahi FD, Danjuma KM, Musa TM, Ibrahim HH. Categorical classification of skin cancer using a weighted ensemble of transfer learning with test time augmentation. *Comput Biol Med*, 2024 Nov; 183: 109378. doi:10.1016/j.compbiomed.2024.109378.
17. Jha DK, Ahmed AEH, Rahman RS. A review on skin cancer and new treatment approach. *Orient J Chem*, 2024; 40(2): 345-356. doi:10.13005/ojc/400215.[HYPERLINK "http: //dx.doi.org/10.13005/bbra/3236" \t "_blank" http: //dx.doi.org/10.13005/bbra/3236]
18. Golestani P, Farjadian F, Ghasemiyeh P, Mohammadi-Samani S. Lipid-based nanoparticles as a promising treatment for skin cancer. *J Control Release*, 2024 Apr; 368: 450-468. doi:10.1016/j.jconrel.2024.02.018.
19. Chatzilakou E, Huang Y, Nguyen J, Athanasiou K, Yang Y. Biosensors for melanoma skin cancer diagnostics. *Biosens Bioelectron*, 2024 Jan; 243: 115741. doi:10.1016/j.bios.2023.115741.
20. Otun SO, Ibrahim A, Vincent O, Okonkwo M. Unveiling the potential of Muscadine grape skin extract as an innovative therapeutic intervention in cancer treatment. *Biomed Pharmacother*, 2024 Apr; 173: 116420. doi:10.1016/j.biopha.2024.116420.
21. Gomes BS, Costa AC, Pereira S, Silva FV, Ferreira VM. Beyond the adverse effects of the systemic route: Exploiting nanocarriers for the topical treatment of skin cancers. *Eur J Pharm Biopharm*, 2024 Feb; 195: 114-132. doi:10.1016/j.ejpb.2023.12.009.
22. Yu Y, Li S, Liu Y, Peng S, Zhang L, Xu L, Yang Q, Du D. Roles of reactive oxygen species in inflammation and cancer. *Mil Med Res*, 2024 Feb; 11(1): 12. doi:10.1186/s40779-024-00489-3.
23. Zhang XE, Peng Z, Sun Z, Yang X, Ma E, Li Y, et al. Microbiome: Role in inflammatory skin diseases. *J Inflamm Res*, 2024 Feb; 17: 1267-1285. doi:10.2147/JIR.S449876.

24. Chang J, Wang BY, Seo MS, Goh M. Nanoparticles as a therapeutic delivery system for skin cancer prevention and treatment. *J Control Release*, 2023 Jan; 353: 221-240. doi:10.1016/j.jconrel.2022.11.028.
25. Di Bartolomeo L, Veronesi F, Neri I, Fabbri B, Lolli P. Wnt signaling pathways: From inflammation to non-melanoma skin cancers. *Int J Mol Sci*, 2023 Jan; 24(3): 2145. doi:10.3390/ijms24032145.
26. Hasan N, Malik AN, Islam MU, Javed A, Shah SWH, Ahmad A. Skin cancer: Understanding the journey of transformation from conventional to advanced treatment approaches. *Cancer Cell Int*, 2023; 23(1): 287. doi:10.1186/s12935-023-03145-8 [https: //doi.org/10.1186/s12935-023-03145-8].
27. Duarte J, Santos A, Espírito-Santo E, Silva F, Dias MB. Topical delivery of nanoemulsions for skin cancer treatment. *Eur J Pharm Biopharm*, 2023 Nov; 192: 98-117. doi:10.1016/j.ejpb.2023.09.011.
28. Chine KA. Review article on skin cancer. *Int J Res Trends Innov*, 2023; 8(4): 245-250.
29. Goyal R, Sharma H, Kaur W, Hasan CR, Patel R. Recent advancements in skin cancer treatment: A critical review. *Explor Med*, 2023 Oct; 4: 624-648. doi:10.37349/emed.2023.00168 [https: //doi.org/10.37349/emed.2023.00178].
30. Zeng L, Hu B, Jiang G, Ma G, Ahmed M, Ali SA. Advancements in nanoparticle-based treatment approaches for skin cancer therapy. *J Nanobiotechnology*, 2023; 21(1): 312. doi:10.1186/s12951-023-02085-4.
31. Yu Y, Li S, Liu Y, Peng S, Zhang L. Roles of reactive oxygen species in inflammation and cancer. *Mil Med Res*, 2024 Feb; 11(1): 12. doi:10.1186/s40779-024-00489-3.
32. Dobre EG, Stoica MC, Căruntu C, Mitran MI, Ailenei A, Costache DO, et al. Skin cancer pathobiology at a glance: A focus on imaging techniques and their potential for improved diagnosis and surveillance in clinical cohorts. *Int J Mol Sci*, 2023 Jan; 24(2): 1458. doi:10.3390/ijms24021458 [https: //doi.org/10.3390/ijms24021458].
33. Khan NH, Malik MM, Lqbal QM, Bukhari MF, Ahmed K. Skin cancer biology and barriers to treatment: Recent applications of polymeric micro/nanostructures. *J Drug Deliv Sci Technol*, 2021 Jun; 64: 102561. doi:10.1016/j.jddst.2021.102561.
34. Krueger A, Zhang J, Schlievert PM, Loughran NB, Schnaubelt M, Tomic-Canic M, et al. Secreted toxins from *Staphylococcus aureus* strains isolated from keratinocyte skin cancers mediate pro-tumorigenic inflammatory responses in the skin. *Front Microbiol*, 2022 Jan; 12: 812041. doi:10.3389/fmicb.2021.812041.

35. Souto EB, da Ana R, Vieira V, Jäger A, Freitas JT, Dias-Ferreira J, et al. Non-melanoma skin cancers: Physio-pathology and role of lipid delivery systems in new chemotherapeutic treatments. *Prog Lipid Res*, 2022 May; 86: 101158. doi:10.1016/j.plipres.2022.101158 [https: //doi.org/10.1016/j.neo.2022.100810].
36. Manzano CM, Hernández D, Nunes R, Escobar F, de Paiva P. Revisiting metallodrugs for the treatment of skin cancers. *Coord Chem Rev*, 2022 Mar; 451: 214264. doi:10.1016/j.ccr.2021.214264.
37. Pfeifer GP, Besaratinia A. Mechanisms of UV-induced mutations and skin cancer. *Genome Instab Dis*, 2020 Mar; 1(1): 99-113. doi:10.1007/s42764-020-00009-x [https: //doi.org/10.1007/s42764-020-00009-8].
38. Matar DY, Boulos N, Obeid D, Mehanna W, Darwiche PO, Abou Chakra C. Skin inflammation with a focus on wound healing. *Adv Wound Care (New Rochelle)*, 2023; 12(4): 215-230. doi:10.1089/wound.2022.0087.
39. Liu R, Qiu W, Ren Z, Huang X, Yang C, Xu X. Risk of non-melanoma skin cancer with biological therapy in common inflammatory diseases: A systematic review and meta-analysis. *Cancer Cell Int*, 2021; 21(1): 467. doi:10.1186/s12935-021-02136-6 [https: //doi.org/10.1186/s12935-021-02325-9].
40. Bernardini N, Segatto M, Emiliani C, Tomassoni D, Marchetti MC, Amantini C, et al. IL-17 and its role in inflammatory, autoimmune, and oncological skin diseases: State of the art. *Int J Mol Sci*, 2020; 21(14): 5077. doi:10.3390/ijms21145077.
41. Ramya Silpa S, Venkat C. A review on skin cancer. *Int Res J Pharm*, 2013 Aug; 4(8): 83-88. doi:10.7897/2230-8407.04817.
42. Maru GB, Gandhi K, Ahuja A, Rastogi K. The role of inflammation in skin cancer. In: Aggarwal BB, Sung B, Gupta SC, editors. *Inflammation and Cancer*. Basel: Springer; 2014; 437-469. doi:10.1007/978-3-0348-0837-8_17.[https: //doi.org/10.1007/978-3-0348-0837-8_17]
43. Ansari KM, Rundhaug JE, Fischer SM. Multiple signaling pathways are responsible for prostaglandin E2-induced murine keratinocyte proliferation. *Mol Cancer Res*, 2008 Jun; 6(6): 1003-1016. doi:10.1158/1541-7786.MCR-07-2173.
44. Cataisson C, Salcedo R, Hakim S, Moffitt BA, Wright L, Yi M, et al. IL-1R–MyD88 signaling in keratinocyte transformation and carcinogenesis. *J Exp Med*, 2012; 209(9): 1689-1702. doi:10.1084/jem.20110554.