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SKIN CANCER - PAST-PRESENT AND FUTURE: A COMPREHENSIVE REVIEW

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Abstract

Skin cancer consists of three major types referred to as Squamous cell carcinoma, Melanoma and Basal cell carcinoma. At present, there is no such applicable and investigated technique for understanding pathophysiology as well as the key biomolecules for the purpose of diagnosis of skin cancer at the level of metagenomics. The key driving mutations that are associated with the progression of this disease are the mutations in the MAPK cascade followed by the mutations in the BRAF gene, this gene is altered at the deepest level along with the loss of function of the tumor suppressor gene, P53 and these two proteins can be used to engineer novel therapeutics against the disease. For the characterization and identification of the key, common molecules researchers are utilizing a new technique, Genetic expression profiling, to understand the types of skin cancer at the molecular level. This method, in combination with the traditional one, allows clinicians to assess the risk in the patients that are susceptible to this disease. By utilization of this technique researchers can identify key patterns of mutations and alterations in skin due to which the cancer metastasizes, and this can also lead towards the development of novel targeted approaches that limit the adverse reaction of the so-called chemotherapeutics. Various efforts and collaborations have been made across the globe to counter skin cancer and hence, in the development of personalized and cost-effective approaches for treating skin cancer.

INTRODUCTION

Damage to DNA leads to the development of tumors and if untreated these tumors grow into cancerous cells that are difficult to treat. These cells grow exponentially and bypass the immune system, that's why these are difficult to detect as well. Although our skin has different layers, but mostly skin Cancer develops in the epidermis, the outermost layer (1). The rate at which this cancer progresses varies with the skin types as well as gender differences. Males are more affected than female and black skin (having more melanin) is less prone to skin cancer than white skin due to a variety of reasons one being the

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exposure to sunlight. However, genetics also plays a critical role in the progression of this disease (2).

Skin cancer is a global concern because of the depletion of ozone layers and the increase in intensity of the ultraviolet rays that promote the formation of tumors inside the different layers of the skin. Although skin cancer is of many types, the most serious one is melanoma as it is not localized and spreads to different organs of the body and that is the reason it is more difficult to deal with. On the other hand, SCC and BCC can be managed if diagnosed at an early stage of development (3). Skin color, gender and the composition of the fats also plays crucial role in the progression of this disease as people with a dark complexion are more resistant to this disease than those with a fair complexion because of the presence of the skin pigments and cell called melanocytes that secretes melanin, which gives skin a dark tone (4).

Genetic Expression Profiling is highly associated with various diseases worldwide. It uses genetic expression patterns of the most important genes that are involve in the development of this specific disease (5). It mainly focuses on the quantification and identification of RNA transcripts in the sample taken from the patients. Furthermore, this technique, combining the microarray analysis, has been very useful for a number of diseases that are being studied on the genomic level as reported in various research articles (6). Genetic expression profiling promises a great deal of opportunities in understanding the level of transcription of the DNA into the RNA following the protein synthesis and the number of transcripts in turns, telling us about the relative expression of the gene. Hence, based on these we can easily differentiate the genes that are up regulated in case of the skin cancer (6).

Skin cancer is regarded as the most common disease in USA, accounting for 20-30% neoplasms in Caucasians, 2-4% in Asians, and 1-2% of all neoplasms in Asian Indians and blacks (7). On the contrary, it is a hectic task to estimate the prevalence of non-melanoma skin cancer because of the lack of proper data and statistics in the national and international registries worldwide. Moreover, the interpretation of histopathological, histo-physiological and differences on the clinical levels is more difficult between different races and ethnic cultures, because the incidence of tumors in Hispanics, Asians and the Black people are smaller than those reported in Caucasians (8).

The main of this article is to review the recent efforts in the management of skin cancer to analyze the trend on a global level and compare it with that of Pakistani population. Moreover, genetic expression profiling has enabled the identification and characterization of the key targets that are responsible for the progression of the disease. Recent advancements in the management of skin cancer are also discussed in this study.

2. Epidemiology

According to the published data, in 1978, incidence melanoma and non-melanoma was 232/100,000 in Caucasians community and 3.4/100,000 in Black community, this data strongly indicated that the Caucasians possesses a high chance of developing cancer than those of the black ones (approximately 70 times more) (7). Since late 1960s, the rate of incidence of basal cell carcinoma and squamous cell carcinoma in the white population have increased considerably at a rate of 6-8% annually (7). On the other hand, the incidence of basal cell carcinoma in the Japanese community have increased from 1977-1982, but the incidence of non-melanoma remained constant throughout this tenure (9). Rate of incidence of non-melanoma skin cancer in the people of Japan is in the range of 1.2-5.4/100,000 (10). According to the recent analysis given by the Singapore Cancer Registry showed that the prevalence of melanomas is increasing at an alarming rate than before, from in 6/100,000 in 1968 to 8.9/100,000 in 1997 (11).

On the contrary, the incidence rate of these types has remained constant in the black community because of their extra melanin inside their body (12). Among, southeast people of Arizona, there was not a slight change in the incidence of any type of skin cancer from 1996-2007 despite the prevalence of skin cancer in men other ethnic groups. The rate of mortality for non-melanoma skin cancer NMSC restricted to a factor of 20- 30% among different communities of United States from 1969 to1988, meanwhile it is seen that the declination of cases among the Blacks were not that consistent as that of the White population (8). Rate of mortality in the

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Blacks, nonetheless, was still high in contrast to the incidence rate. The data on the mortality and incidence rate is not as easy to access because of the prevalence of Kaposi sarcoma that is closely linked with AIDS in the late 1990s.

Across the international community, Melanoma stands 5th among the most common cancers and accounts for almost 6.1% of the cancer incidence (melanoma being 1.7%) with an overall mortality rate of 0.5-0.7% (13). Skin Cancer is one of the most frequent detected skin cancers internationally and ranks 5th in Pakistan. In Pakistan, although there is no authentic registration system for the cancer, but regional cancer registry of the Punjab has taken a step towards the reporting of the high incidence rate of melanoma in response to the Global report of 2018 which states non-melanoma as the 18thand melanoma as the 32nd most frequent cancer prevailing in Pakistan. Males are more affected by this cancer due to various reasons (14). Furthermore, Registry of Karachi (KCE) has reported skin cancer as the 8th leading in females. According to Dow University of Health Sciences (DUHS), non-melanoma is regarded as the fifth most commonly diagnosed skin cancer in the patients of Karachi and nearby areas and the incidence is increasing daily (15).

Considered, the incidence of skin cancer is increasing at an alarming rate in different regions of Pakistan. So, there is a desperate need to overcome this issue as quickly as possible. Although Pakistani researchers are trying their best to identify novel and key targets that are therapeutically and prognostically significant that can enable the scientists to develop effective treatments regarding this cancer. Figure 1 shows the estimated deaths and new cases of cancer in 2018 and the incidence of melanoma was 5% while its death rate is not as high as others (10). Figure 1 shows the latest trend in skin cancer across both genders as per the statistics from 1975-2017 (10, 16)

3. Types and Associated Risk Factors

Although there are a lot of types of skin cancers based on specific prognosis and characteristics but most of the cases of skin cancers are related with their three major types, Melanoma, Basal Cell Carcinoma and Squamous Cell Carcinoma, categorized into melanoma, the deadliest among all types, and non-melanoma (17). Explanation of all the main types is given below.

3.1 Basal Cell Carcinoma

Basal cell carcinoma is identified as the most common and frequent occurring type of skin cancer in the international community comprising about 80% of all the cases of skin cancer. This specific type of cancer arises in the basal cells, that are the deepest layer of the cells in epidermis, and there are high chances that this tumor can re-appear even though it has completely healed (1, 15). Usually, Basal cell carcinoma is characterized by the appearance of red-color spots on different areas of the skin including scalp and face. Although the rate at which it spread is a lower than the two other types but still it can metastasized to other organs (5). Most of the time, it is associated with the damage in DNA caused by ultraviolet radiations from the sun and without any proper care it can metastasized to other organs but the chances are rare (18).

The rate of incidence of Basal cell carcinoma in different races, per one million, is given below and most of the people affected by this cancer are Hispanics, Caucasians ,Japanese and the Chinese Asians (7), (9, 11). Black males (1) and black females (2), Africans residents that are Kenyans (0.065), Chinese men and women, 6.4 and 5.8 respectively, and almost 30% in residents of Okinawa and Kawaii along with an average of 250 cases in Caucasians (19). Contrary to this, it is highly prevalent in the Asian Indians and Blacks and there are rare chances of this type to occur in the blacks while most of the times white are more affected (20). With respect to data collected from different medical centers, the prevalence of Basal cell carcinoma accounts for 2-3% of the total annual cases (7). The figure below shows cancer on different skin types (21). The incidence of this cancer is highly dependent on the age factor and it advances with the increase in age and approximately 40% of the patients that are diagnosed with this disease develops more lesions within the next 4-6 years (18, 22).

The etiology of basal cell carcinoma is given below:

- Exposure to ionizing radiation.
- Sebaceous Nevus

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- Previous history of sunburn
- Age and genetic factors
- Exposure to arsenic
- Gorlin's Syndrome, a disease characterized by the autosomal mutation of the patched human gene (23).

3.2 Squamous cell carcinoma

The incidence of squamous cell carcinoma is comparably less than that of the BCC and this develops in the specific skin cells called squamous cells. This type usually appears on those areas of the skin that have rough appearance overall (24). But in some cases, it can also appear on those body parts which are periodically exposed to sunlight and appear on skin as Blackish-yellow or red colored spots. The occurrence percentage of SCC is 22% more than that of BCC as reported in a study conducted in the United States (25). Just like the basal cell carcinoma, it can also metastasize to other body parts but various treatment modalities have been developed that effectively fights off this specific type of skin cancer (18).

It is considered as one of the predominant diseases in Indians and blacks accounting for more than 55% of the cases in both the communities (7). Whereas, it is also regarded as one of the common kind of tumor associated disease in the Caucasians accounting for almost 30% of the total skin cancer related cases (26). The rate of incidence of SCC is, on average, 300/100.000 per male and females in Caucasians and 118/100,000 in the locals of Kawaii and almost 23/100,00 in those Japanese that are the residents of Kawaii (22). 21/100,000 in case of New Hispanics residents of Mexico and approximately 25/100,000 in case of Hispanics that lives in Southeast Arizona (27).

The etiology of SCC is given below:

- Localization and recurrence of tumor.
- Poorly defined borders between countries
- Lack of immunity
- Chronic inflammation
- Symptoms of neurological conditions
- Perineural involvement

3.3 Melanoma

This specific type of cancer is very rare but considered the most dangerous of all the types. This develops in the melanocytes, melanin producing cells, that give skin is dark complexion and protect it from the ultraviolet rays coming from the sun (4). It's considered fatal because of its ability to metastasize other organs at a higher pace than the Squamous cell carcinoma . It can develop in all types of ages, but mostly affected individuals are the aged one, but on the other this cancer can be diagnosed at an early age so effective treatment can be given to neutralize it (28). When melanoma are exposed to ultraviolet radiations for too long, chances are there may develop a mutation in the DNA that may result in the high expression of the oncogenes, which is accompanied by the lack of functioning of the tumor suppressor genes (18). Prognosis of this specific type of skin cancer is related to the depth as well as the location of the primary tumor, from where it originated, and the absence or prevalence of the metastasized previous state (6). The picture below shows the dominant types of skin cancer.

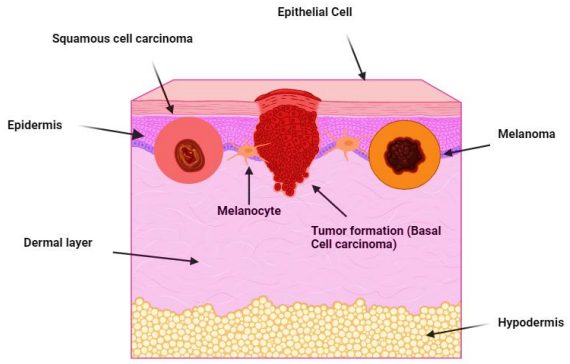

Figure 1: The most prevalent types of skin cancer in human beings.

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Melanoma is the 6th most common cancer globally; its incidence is higher in the European region, as the spread of this type is more contagious than the preceding two. The estimated rate of diagnosis and incidence will increase by 7 to 50 patients by the end of the 2030, as it was 4 to 50 in the year 2005 (29). In Blacks, Asians and in the Hispanic people, it is regarded as the 3rd most common type of skin cancer malignancies, representing a total of the 8% in Blacks, approximately 14% in the people of Asian Indians, a total of 18% in the Japanese people (10, 27). The ratio of melanoma among the Blacks and the White people is almost 1 to 16 and the range of incidence of the melanoma is a bit higher in the Caucasians (19.8/100,000) than in the Blacks (1.5/100,000) and in correspondence to this, melanoma is roughly 18 times more in the Caucasians (8). On contrary to this, Hispanics have less incidence of this disease (5/100,000) and this shows that Hispanics are 7-10 times more resistant to this cancer than the Caucasians.

Table 1: Comparison of different types of skin cancer

Sr No	Types	Growth	Appearance	Occurrence	Treatment	References
1	**Basal cell carcinoma**	Basal cells of Epidermis	Open sore, non-lethal and have small pinkish growth	Less Severe but more widely occurred than other types (on face and neck region)	Photodynamic therapy, immune-modulating creams or surgery for large	(30, 31)
2	**Squamous cell carcinoma**	Skin squamous cells	Worth, moles and easily bloody patches	More severe but Less occurrence than basal cell carcinoma (on neck, head and arms)	Surgical excision, radiation therapy or Mohs micrographic surgery	(32, 33)
3	**Melanoma**	Melanocytes	6mm size, asymmetrical and multi-colored	Most deadly but rarely occurs than other types (on legs, back, sole of the feet, arms, and scalp)	Cryosurgery surgical removal and creams.	(34, 35)

The etiology of melanoma is described below:

- Presence of nevi
- One or more than one atypical nevus
- Light skin
- More exposure to sunlight
- Sunburn history
- Tanning bed exposure
- Age greater than 65
- Family history

The danger associated with melanoma is the mortality rate that is increasing worldwide, although early diagnosis can lead to favorable outcomes, because of its progression by viewing the data from the literature. Rate of mortality has increased from the past few decades and it was recorded as 34% from 1973-1992 and the rate is expected to increase by the factor of 5% by the end of 2035 (18). But mortality rate differs in different races, but mostly affected are the Caucasians as described above, because of various prevailing reasons the most common one is the presence of the pigment, melanin, that protects from the sunlight (4). Melanin

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is the key agent in the case of melanoma, because any alteration in the DNA of the melanocytes may lead towards the uncontrolled growth of the cells that forms a tumor and that tumors grows into cancer (4, 36).

4. Pathophysiology of skin cancer

Pathophysiology is the combination of two terms, pathology (study of any disease) and physiology (normal functions of the body). It refers to the study and description underlying mechanisms that are being dysregulated and causes are involved in the progression and spread of this diseases, in this typical scenario, skin cancer (37). It is based on the examination and comparative analysis of the normal body functions with that of the disease at the levels of molecules and cells, eventually checking the expression patterns of the abnormal genes and access how these genes are responsible for the disease (38). The main thing that drives the development of normal cells into cancer cells is the mutation and after that the cells metastasize to different sites leading to uncontrolled cell proliferation (37). The pathophysiology of various skin cancers is given below:

4.1 Dysregulation in BCC:

Too much exposure to sunlight is the most dominant risk factor responsible for the BCC. Direct DNA damage is responsible for the development of basal cell carcinoma, accompanied by the indirect damage to the DNA through the suppression of the immune system and ROS (5, 39). Melanin also plays the role in indirect damage by the absorbance of UV-A radiation and cause damage to DNA while UV-B is responsible for the direct damage to the RNA and DNA with a transition of the CC/TT (4, 40). Exposure to ultraviolet radiation also causes immune suppression of cutaneous cells leading to the dysregulation of the immune system. According to studies published in the near past, BCC arises in those cells that are immature or are transiting from the immature to mature stage, cells that are related to hair follicles. One of the key genes that are dysregulated in BCC is PTCH1 and mutation in this gene is associated with 70% of the cases of BCC while 20% of the patients of this type depict the mutation of the SMO gene (30). The inactivation of the PTCH1 or the high expressions of the Gli, by the trans activation of the smoothened is good enough to drive the progression of the basal cell carcinoma. Second most common dysregulation in basal cell carcinoma is the mutation in the gatekeeper gene P53 (41).

Hyper-activation of the Hedgehog (HH), in correspondence to the canonical hedgehog, is the most common hallmark in studying the progression of the basal cell carcinoma as reported by various studies conducted in the past (42). This pathway plays the most critical role in cell proliferation, differentiation, and embryogenesis in the early stages of cell development; this facilitates the development of epidermis by the crosstalk between the dermal cells of the skin and those cells that are of epithelial origin. Canonical activation of the pathways is driven by the ligands names as sonic hedgehog (SHH), Indian Hedgehog (IHH) and sometimes by the Desert Hedgehog (DHH) in response of the PTCH1 receptor (38, 43). Activation of this pathway does facilitate the activation of the SMO, and this SMO migrates to one of the highly specialized primary cilia and as a result, SMO drives the hyper-activation of the Gli transcription factors followed by the suppression of the fused (SUFU). However, if the HH does not attaches with the PTCH1, the Gli family of the transcription factors are in their inactive form as SMO does not translocate to the primary cilia and the Gli proteins are ubiquitinated (5, 38). The eventual results from the activation of thus signaling cascade is dependent on differentiation and proliferation, self-renewal, cell survival (by the activation of the BCL-2 protein family), transition from epithelium to mesenchymal cells, angiogenesis, and invasiveness of the BCC (44). However, in case of the non-canonical signaling, HH interacts with a lot of other signaling networks that are oncogenic in nature, such as IGF, TGFβ, aPKC, NF-kB and EGFR (epidermal growth factor receptor); these pathways synergistically contribute to the progression of basal cell carcinoma. It means that, the activation of the Gli family of the receptor may be done by many alternative pathways that are non-canonical but all this happens in the absence of the bypassing of the SMO (45, 46). The activity of Gli is positively influenced by the RAS, PI3K and AKT while it is negatively regulated by the P53

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family of proteins and significantly the expression of the RAS/RAF cascade that further hyper-activates the JUN complex that causes the progression of the developmental processes (6, 47). TGF-beta signaling do activates the upregulation of the GLI2 transcription while GLI1 is activated by the complex protein, aPKC. Furthermore, IGF-1 causes the induction of the nuclear localization of GLI1 and 2 and it have also been observed that the activation of the PI3K and AKT regulates the epithelial-mesenchymal transformation and the secretion of the MMP's (matrix metalloproteins) (47).

4.2 Dysregulation in SCC

Many pathways have been studied to show dysregulation in the pathogenesis of the squamous cell carcinoma and all these forms a network of complex interchanging proteins and genes. The overall development and presentation of this type is a multistage process that involves a lot of mutations in the epidermis of the skin leading to the dysregulation in the normal homeostasis and the proliferation of cancer at an alarming rate (40, 48). Genetic mutations in the TP53 gene are mostly seen in the development of SCC (rate of mutations of this type is comparably larger than the other two main types). P53 is the protein that is encoded by the TP53 gene, that plays the most critical role in the development as well as sustainability of the genome, hence regarded as the gatekeeper gene (guardian of the genome), this protein also performs several other functions like inducing apoptosis, arresting cell cycle, DNA repair or cell senescence (49).

The suppression of this protein in this typical scenario is guided by the mutations occurred bh the viral infection (infection with Human Papilloma Virus E6) followed by the mutations " hot spots", due to the exposure to UV light that causes the exponential expansion of the mutated clones of the TP53 that hinders the normal cell death process (49). Researchers have clearly mentioned the effects of UV-B on carcinogenesis on animal models .

Dysregulation in the TP53 is the first event in the pathogenesis of the SCC, usually in 85% of the cases, and regarded as the main reason in contributing the instability of the genome. Moreover, mutations are also reported in the literature regarding the development of mutations in the late as well as early stages of the SCC (40). The skin that is largely exposed to the UV radiations do have a lot of big lesions that carries the mutation in the gatekeeper gene (TP53) and this mutation can increase over time and according to some previous studies, high mutations are linked with the metastatic tumors rather than the primary tumors (40, 49). Other altered pathways are NOTCH signaling pathway, RAS/RAF pathway, RIPK4 kinase, mutations in EGFR followed by the hyper activation of the PI3K pathway.

4.3 Dysregulation in Melanoma

Various endogenous and exogenous triggers are responsible for the transformation of this specific type of skin cancer by activating a complex network of interconnected pathways that have a complex nature. Although the rate of division of the melanocytes is comparably less than other cells but this rate increases with the increase in size of neoplasm (35, 50). This increase in size itself is accompanied by various factors but the most dominant ones are alterations in the copy numbers and point mutations and in on o the recent publications, researchers concluded that the rate of mutational load on melanoma is high (10/mega base pair) and there is also a large number of mutations caused by ultraviolet radiations (cytosine to thiamine or guanosine to thiamine depend on either the radiations are UV-A or UV-B) (35, 51). Direct and indirect mutations are associated with the progression of melanoma, directly involved from the exposure to UV radiation and indirect arises from the interaction between the melanin (pigment from melanocytes) and UV-A radiation. The transformation to malignant melanoma is accompanied by the cross-talk in different pathways (sequential genetic alterations) as a result of which various oncogenic signals are activated, just as seen in other two forms (51, 52).

The most common mutation is because of the genetic changes in BRAF that further propagates and forms lesions, while the formation of in-situ melanoma requires several more mutations other than the BRAF (alteration in the TERT promoter) (35, 53). However, invasive potential of melanoma is due to the mutations in those genes that control cell cycle, Cyclin-dependent (CDKN2A), and those genes

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that are involved in remodeling of the chromatin, (ARID1A, ARID1B) (52). Although these mutations play key role in the spread of melanoma but the mutations in PTEN and P53 are the major driving mutations that gives melanoma its metastatic potential (mutations in these genes are responsible for the invasiveness of the melanoma) (50). On the level of proteomics, genetic alterations in these genes are provides an over stimulating effect followed by the hyper-activation of the MAPK cascade, PI3K pathway, AKT, and mTOR pathways (35).

Melanoma could evade the immune cells by altering the checkpoints that are crucial in defending the body against attacking microbes. Several notable pathways are involved such as; JAK, the interferon, and STAT transducer pathways are the main driving player of programmed death ligand-1 receptor mediated immune checkpoint (52). Upon binding of the key ligands on the receptor, interferon is released that regulates the expression of the PD-L1 and PD-L2 (by the expression of the JAK/STAT pathways) on the membrane of the cells (41, 50). Binding of both the ligands to the receptor PD-1 leads to the ineffectiveness of the immune cells on the tumor and hence suppress the immune response and further suppression is due to down regulation of the MHC-1 complex along with certain tumor associated antigens (35). The figure below gives a generalized overview of the progression of skin cancer, the main driver of which is sunlight and certain carcinogen that disrupts DNA, ultimately leading towards metastasis.

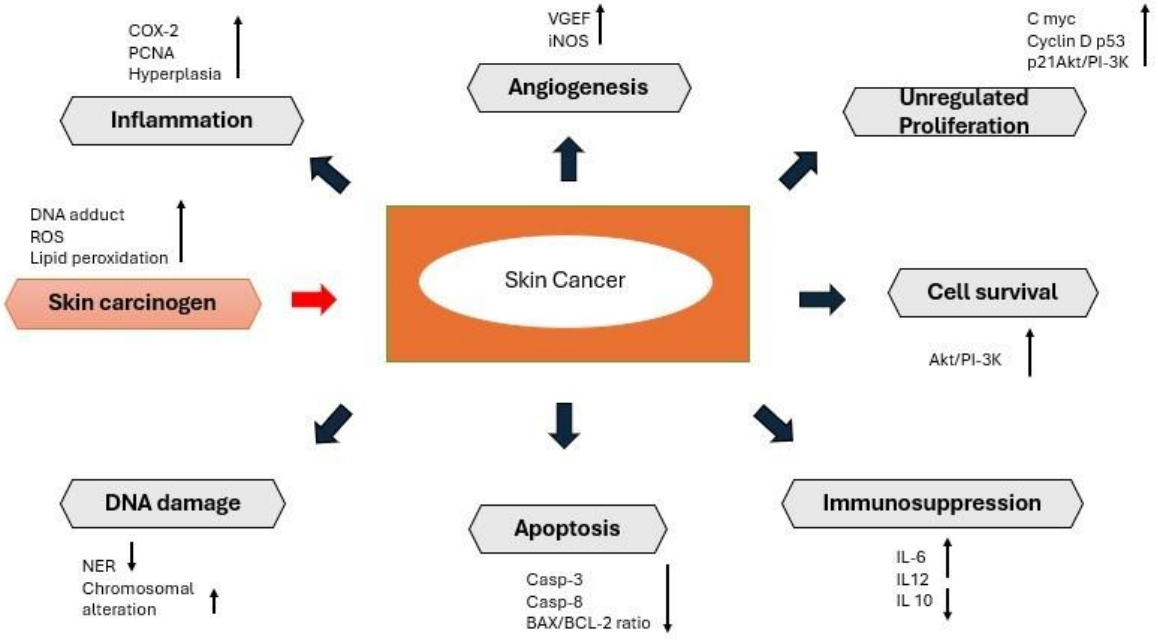

Figure2: Alteration in different upstream and downstream regulators that are involved in skin cancer progression and metastasis.

5. Diagnosis

Alternative diagnosis is considered in case of skin cancer because, multiple conditions are associated with such as various benign conditions like; seborrheic keratosis, verruca vulgaris, actinic porokeratosis, eczema, psoriasis and lichen planus whereas, malignant conditions like SCC, BCC, Bowen's disease, lentigo maligna, extramammary Paget's disease and keratoacanthoma are also associated with it (54). A complete examination of the body is recommended in case of skin cancer for those individuals that are at a greater risk of developing the disease (that have lesions on their skin) (55). For some skin cancers, use of non-invasive technologies like dermascopy (based on the visualization of the skin's epidermal layer and

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border) and optical coherence tomography (testing of retina with the help of light waves) are considered to enhance the overall accuracy. For the identification of the actinic keratosis, photodynamic visualization would be a better option as it is based on the visualization of skin with the help of light exposure to the 5-aminolaevulinic acid (56).

In the case of basal cell carcinoma, dermascopy can be useful in the diagnosis and differentiation of the non-pigmented BCC from the pigmented ones. This is characterized by the development of arborizing vessels and globules of blue-gray colors with a leaflike structure. Differential diagnosis is sometime confused with the diffusion of trichoepithelioma while superficial basal cell carcinoma have the ability to mimic some inflammatory conditions like eczema and psoriasis (57).

Squamous cell carcinoma shows yellow crystals that are opaque (transparent) in nature (dotted and coiled vessels having bumpy appearance). Clusters of both the two types are distributed in the small dense groups characterized within the same lesion (55, 58). Pigmented Bown disease shows globules of brown color that are small and aligned in regularly packed distribution throughout the skin while early SCC and keratosis are characterized by white circles with a targetoid and ring like structure (58). Apart from the techniques described above, some other techniques are also employed for the imaging of squamous cell carcinoma including, Reflectance Confocal Microscopy (techniques employs non-invasive technology for the imaging of skin, having the resolution of 0.5- 5 mm, using light of wavelength 830 nm (in near-infrared region)), High frequency ultrasonography and doppler mode (non-invasive, easy, fast and accessible technique that is practiced worldwide for the early diagnosis of SCC, it allows provides minor details in real-time using frequency of almost 20 MHz that enables the scanning of all the layers of skin) (55, 59).

The diagnosis of melanoma was accessed by the light imaging technologies for the first time back in 1990's and it was thought that surface microscopy should be practiced at large (technique is based on the layering of skin lesion on glass slides and put a drop on it and see through stereo microscope) for the best result but was very time consuming (28). To overcome this drawback, dermascopy was established and is now the most accepted technique that have the ability to either increase or decrease the chances that the lesions are either malignant or benign (uses a light magnifier that allows the clinician to see 10-fold) (60, 61). The main drawback of dermascopy is its failure to screen featureless forms of melanoma. Other techniques that are recently employed for the diagnosis of melanoma include; Digital Image Capture and Analysis, Computer-Augmented Image Analysis, Multispectral Digital Dermascopy, Confocal Scanning Laser Microscopy, Reflectance Confocal Microscopy, Optical Coherence Tomography And Cellular Electrical Resistance (differences between impedances of normal skin and benign lesions of melanoma) (37).

6. Treatment

Multiple treatment options are considered nowadays because of the higher rate of malignancies of cutaneous forms of cancer and the choice of which technique is to be used depends on the degree of progression, margins, dimensions, and location of the lesions (59). However, surgical treatments including excision biopsy is considered as the "gold standard" in managing skin cancer and this treatment option is primarily based on 3 outcomes, preservation, complete eradication and cosmesis (restoration or preservation of physical appearances and it is quite often related with improvement of skin aesthetic aspects) (55, 62). Other common methods for the treatment are, Cryotherapy (clinician uses liquid nitrogen for freezing the cancer cells and dead cells are then sloughed off at the end of the treatment), Excisional Surgery (clinician go for the surgical removal of the damaged skin area to ensure all cancerous cells are cut), Mohs Surgery (clinician go for the removal of only damaged area of the skin, trying to save normal ones as much as possible, this approach is mainly done for the squamous and basal cell carcinomas or sometime to those types that are prevalent in critical areas like lips, forehead, ears, eyelids, your scalp or near to genital areas), Curettage and Electrodesiccation (clinician uses a tool with sharp edges to cut out the diseased cells and after that they destroy the remaining cancer cells with the help of an electric needle; technique is mostly used for the treatment of precancerous cells along with squamous cell

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carcinoma), Chemotherapy (this treatment modality is based on the use of medicine (either in the form of pills or ointments) for the destruction of cancerous cells (63), in some cases IV is considered if the cancer has metastasized to other body parts), Immunotherapy (clinicians targets the immune cells of the patients, by using medicine, to fight the disease) (64), Radiotherapy (clinicians uses strong beams of radiations to either kill or to stop the growth of cancer cells), Photodynamic Therapy (clinician uses ointment son the skin and then activates the medicine with the help of beam of light (blue or red color light is used) is used for the destruction of precancerous cells in squamous and basal cell carcinoma and does not have any effect on the surrounding cells) and Biological Treatment (this treatment stimulates the immune cells of the patient to fight of the disease by using biological therapy) (18, 22, 65). Cancer can be treated with modern therapies because of advancement in medical field (66). Computer aided studies of proteomics or genomics may be helpful for cancer treatment (67). Treatment procedures along with proper diet plan and regular physical activities regulate body to cure and prevent form infections (34).

7. Conclusions

Skin cancer does occur in the people with dark skin color and poses notable risk to health. Skin cancer in colored people have high mortality and morbidity rate than in SCC, cutaneous T-cell lymphoma, Caucasians, melanoma, and potentially KS exhibit poor prognosis. Healthcare providers should take measures for the prevention of individuals with ethnic backgrounds facing skin cancer. Promoting awareness among the communities, self-examination, and regular examination of skin can facilitate earlier skin cancer diagnosis because of which the rate of mortality and morbidity in different ethnic groups decreased.

Conflicts of Interests

The authors declare no conflict of interest in relation to this review paper.

Authors Contribution

All the authors contributed equally in this publication

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