www.directivepublications.org

Journal of Cardiovascular Diseases

ISSN 2831-3437

DIRECTIVE PUBLICATIONS

Review Article

A Review of Major Skin Cancers: Physiology, Diseases, Market Analysis, and Treatments.

Sophia Welsh, Tawil, Bill

Affiliations:

[1] *Department of Bioengineering, University of California, Los Angeles (UCLA), USA.*

Running Title: A Review of Major Skin Cancers: Physiology, Diseases, Market Analysis, and Treatments.

Abstract

Skin cancer is one of the most common cancer types, affecting approximately 20 percent of Americans throughout their lifetime. There are a multitude of types but the majority of skin cancer cases are one of three types: Melanoma, Basal cell carcinoma, and Squamous cell carcinoma. Like most cancers, early detection for skin cancer and access to proper treatments are keys to increasing survival rates. Constant interest in increasing survival rates have led to the combined skin cancer diagnostics and treatment market to have grown to 19.83 billion USD market size as of 2023. The diagnostics are visually based and encompass both a doctor assessment and an additional biopsy for closer identification. The variety of treatments are more extensive than the common diagnostic techniques and include drugs, radiation, and surgery. This review aims to increase understanding of the three major skin cancer types better, including the physiology of the healthy skin, the causes, risks, and detection of skin cancer, the physiology of each different cancer type, the market size, segments, and trends of skin cancer, the current available treatments - both commonplace and tissue engineered, the possible treatment options in clinical trials and being researched.

Keywords : Skin cancer, melanoma, Squamous Cell Carcinoma, Basal Cell Carcinoma, Tissue Engineering.

INTRODUCTION

Skin cancer is one of the most common types of cancer, affecting approximately 20 percent of Americans over the course of their lives (1). There are three main types of skin cancer: melanoma, basal cell carcinoma, and squamous cell carcinoma (2). Basal cell carcinoma (BCC) is formed in basal cells in the lower part of the epidermis (3). Squamous cell carcinoma (SCC) forms in squamous cells on the outer layer of the epidermis (3). Melanoma forms in melanocytes, the cells which produce melanin (3). In addition, there are four less common types, including Kaposi sarcoma, Merkel cell carcinoma, sebaceous gland carcinoma, and dermatofibrosarcoma protuberans (3).

While ultraviolet (UV) light exposure is a primary cause of skin cancer, areas of skin not typically exposed to sunlight can still be affected (1). Several other risk factors also contribute to the likelihood of developing skin cancer, which will be explored in more detail when discussing the physiology and pathology of the disease. This review will focus on treatments for the three most common types of skin cancer, with particular emphasis on melanoma, as it is the most dangerous form (1). We will examine the physiology of the skin, the cancer stages associated with melanoma and nonmelanoma types, current standard and tissue-engineered treatment options, and provide an in-depth analysis of the skin cancer market, including size, distribution, and emerging trends.

Physiology of Healthy Skin

The skin is the body's largest organ, making up approximately 16% of the human body weight (4). It is composed of water, proteins, fats, and minerals, acts as a barrier against germs and environmental elements, regulates body temperature, and contains nerve endings that help detect sensations such as heat, cold, and pain (5). The skin is also important for the synthesis of vitamin D (4). It is composed of 3 layers including the epidermis, the dermis, and the deeper subcutaneous tissue or the hypodermis (6).

The outermost layer, the epidermis, continually renews itself and houses melanin, the pigment responsible for skin color

***Corresponding Author:** **Dr. Bill Tawil**, Department of Bioengineering, UCLA School of Engineering, 420 Westwood Plaza, Room 5121, Engineering V. P.O. Box: 951600, Los Angeles, CA 90095-1600, USA. **Fax:** (310) 794-5956, **Email:** bill.tawil@csuci.edu.

Received: 03-July-2025, Manuscript No. JOCD - 4959 **; Editor Assigned:** 04-July-2025 **; Reviewed:** 17-July-2025, QC No. JOCD - 4959 **; Published:** 22-July-2025, **DOI:** 10.52338/jocd.2025.4959.

Citation: Dr. Bill Tawil. A Review of Major Skin Cancers: Physiology, Diseases, Market Analysis, and Treatments. Journal of Cardiovascular Diseases. 2025 July; 12(1). doi: 10.52338/jocd.2025.4959.

(4). It contains Langerhans cells, a dendritic antigen presenting cell, which play a role in immune defense, Merkel cells, cells that receive the sensation of touch and contain substances that act as hormones, and sensory nerves (4) (7) (8). More importantly for this review, it contains melanocytes, which are the cell type in which melanoma develops (9). For thick skin it can be up to 1.5 mm thick while it can be as thin as .05 mm thick (9). It is further divided into either four or five layers depending on the thickness of the skin (6). For thin skin with only 4 layers these include: stratum basale, stratum spinosum, stratum granulosum, and stratum corneum (6). For thick skin, like that on the hands and feet, there is an additional layer called the stratum lucidum (6). The innermost layer is the stratum basale or stratum germinativum which is composed of basal cells (8). These cells continually divide and push up older cells into the stratum spinosum or the squamous cell layer (8). The cells here are now known as squamous cells or keratinocytes which produce the protective protein, keratin and are held together by spiny projections (8) . These keratinocytes are further pushed up into two thin layers, the stratum granulosum and the stratum lucidum, flattening, enlarging, and adhering the cells together (8). These cells will eventually dehydrate and form a tough durable material which migrates to the surface of the skin (8). The outermost layer, the stratum corneum is the layer of dead keratinocytes which sheds and is constantly replaced by new layers of tough durable skin (8).

Beneath the epidermis lies the dermis, which makes up the majority of the skin's thickness (5). This layer is a fibrous structure that provides strength and elasticity through collagen and elastin, holds hair follicles and nerve endings, produces oil and sweat, and supplies blood to the epidermis (10). The dermis is composed of 2 layers: the papillary dermis and the reticular dermis (10). The papillary dermis is the top layer of connective tissue formed of a loose mesh of collagen and elastin fibers (11). It holds fibroblasts, a small number of fat cells, adipocytes, the immune cell phagocytes, lymphatic capillaries and numerous small blood vessels (11). Below this lies the reticular layer which is considerably thicker and is composed of dense, irregular connective tissue (11). It similarly holds numerous small blood vessels and has numerous sympathetic nerves as well (11). In this layer collage provides the strength and tensile strength that allow for movement and also for water retention (11).

The deepest layer is the hypodermis, a fatty layer, which serves as insulation, cushioning for muscles and bones, fat and energy storage, and provides a pathway for nerves and blood vessels to travel to the upper layers (5) (12).

Melanoma, Basal Cell Carcinoma (BCC), and Squamous Cell Carcinoma (SCC) causes, risk factors, detection

Causes

Melanoma and nonmelanoma cancers like basal cell carcinoma and squamous cell carcinoma are the uncontrollable division of mutated cells in the epidermis including basal cells, squamous cells and melanocytes (13). They are largely caused by Ultraviolet radiation (UVR) which causes DNA damage, gene mutations, immunosuppression, oxidative stress and inflammatory responses and can be split further into UVA and UVB (13). UVB produces DNA damage through the formation of cyclobutane pyrimidine dimers, which are also highly mutagenic (14). This is especially dangerous since it can create mutations in the p53 tumor suppressor genes, which are involved in DNA repair and cell apoptosis (13). UVA on the other hand plays a role in the carcinogenesis of stem cells of the skin (13).

Risk factors

Pale skin is commonly associated with higher risk of skin cancer (13). This is due to the lower inherent sun protection factor in the epidermal melanin of people with lighter skin colors (13). The more melanized a melanosome is, the larger and better scattering ability it has (13). This means that people with higher levels of melanin, those with darker skin are able to scatter more UVB radiation than those with light skin (13).

Other than just pale skin, other physical attributes like light hair and eye colors and freckles increase risk of developing skin cancers (15). To be specific, having light eye color (blue or green) is associated with an approximately 50% increased risk of developing melanoma (15). Having light-brown hair is associated with an approximately 60% increased risk, having blonde hair poses an almost double risk and having red hair has similar if not increased risk as those associated with blonde hair (15) . Lastly, freckles at least in high-densities are associated with greater than double the risk (15).

Another risk factor includes UV exposure both from the sun and from unnatural sources (16). Given that UV radiation is the main cause of skin cancer, increasing the exposure to it, leads to higher rates of skin cancer (16). Case controlled studies and meta-analyses have shown that Melanoma, BCC, and SCC risks are increased in people who have ever used a sunbed even if they have not been burned while doing so (16).

Additionally, genetics and family history play a role in increasing risk of developing skin cancers (17). Researchers have identified numerous inherited genes which were present in families with histories of developing skin cancer, including the CDKN2A or p16 gene, the MC1R gene which is

also associated with fair skin and red hair, the MITF gene and the TERT gene (17). Besides the genetic basis, there is also an increased risk of developing skin cancer for those with first degree relatives who had cancer, with around 1 in 10 people who have melanoma having a family history of the disease (18). This has been linked back not only to genetics but also to the tendency for skin color and lifestyle of sun exposure to be fairly consistent within families (18).

The last notable risk factor is having a compromised immune system, either due to a congenital disorder or due to HIV (18). This is due to the lack of a strong immune system to fight off the cancer and it affects cancers of other organs as well as skin (18).

Detection

To determine if a patient has skin cancer usually a skin cancer screening exam is performed by a doctor (19). During this exam, a doctor reviews the skin for signs of actinic keratoses, which are precancerous, BCCs, SCCs, and abnormal moles which could indicate melanoma (19). If a suspicious growth or mole is found, the doctor will either remove it and send it in for biopsy or monitor it (19). For determining if a growth is suspicious doctors follow the ABCDE rule (3). Here A stands for asymmetry where they review the growth for an irregular shape (3). B stands for border, where blurry or irregular shaped edges breed concern (3). C stands for color, where multicolored moles are cause for concern (3). D stands for diameter and a large diameter would indicate a suspicious growth (3). Lastly, E stands for evolution and the change in the growth's appearance is heavily monitored as the most important indicator of skin cancer (3).

If the doctor decides to send a sample in for a biopsy, they will take the sample and send it to a lab where it will be viewed under a microscope to identify cancerous cells (21). There are multiple types of biopsies that might be performed including: a shave biopsy where the top layers of skin are shaved of, a punch biopsy, where a round section of the skin will be removed with a special tool, and lastly an excisional biopsy where the entire lesion is removed (21). The choice of which biopsy is decided by the doctor and it will depend on location, size, and depth of the suspicious area (21).

Figure 1. Diagram of the different layers of the skin.

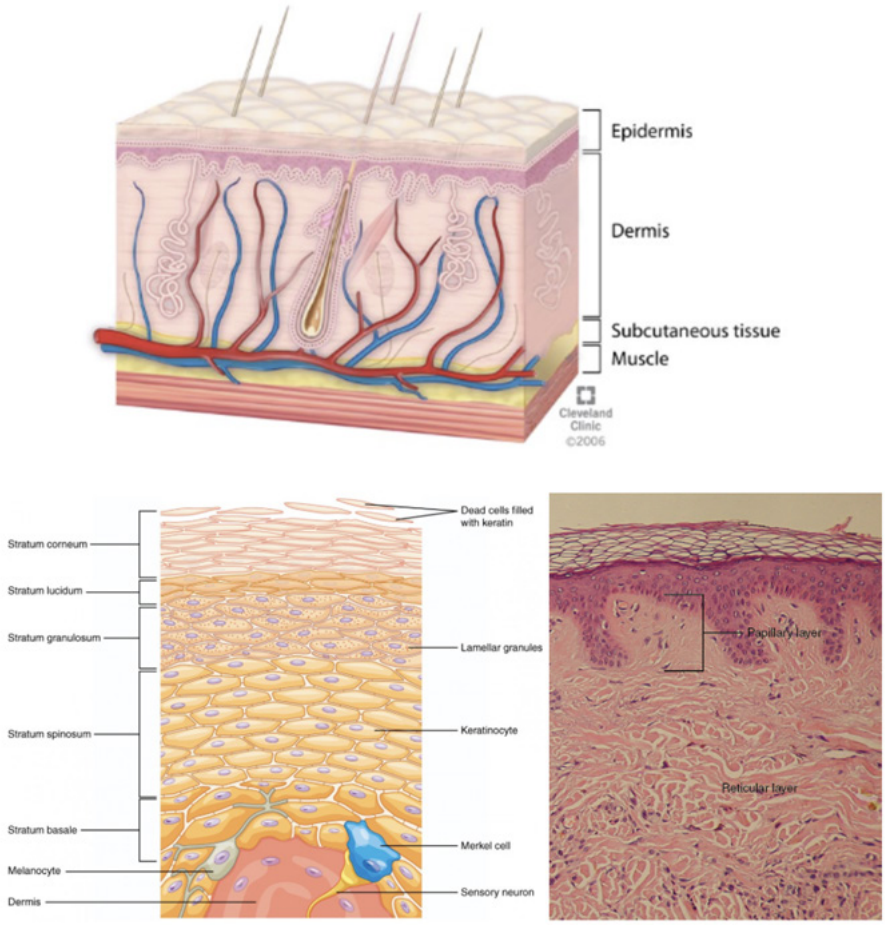


Figure 2. Major Risk Factors associated with skin cancer

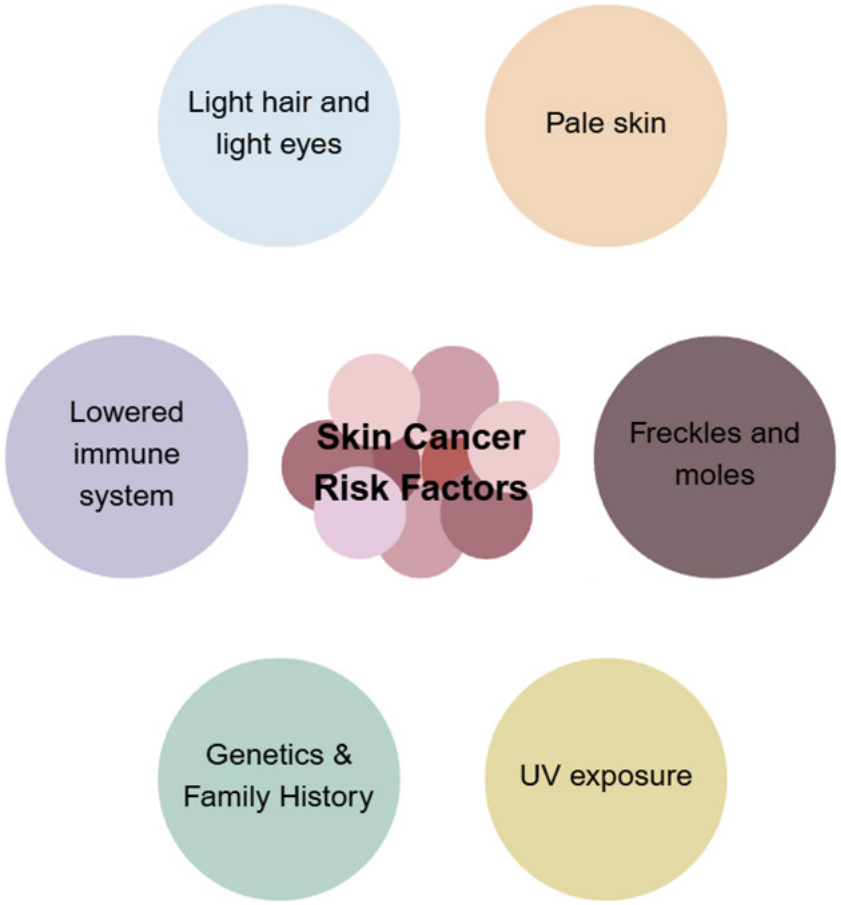
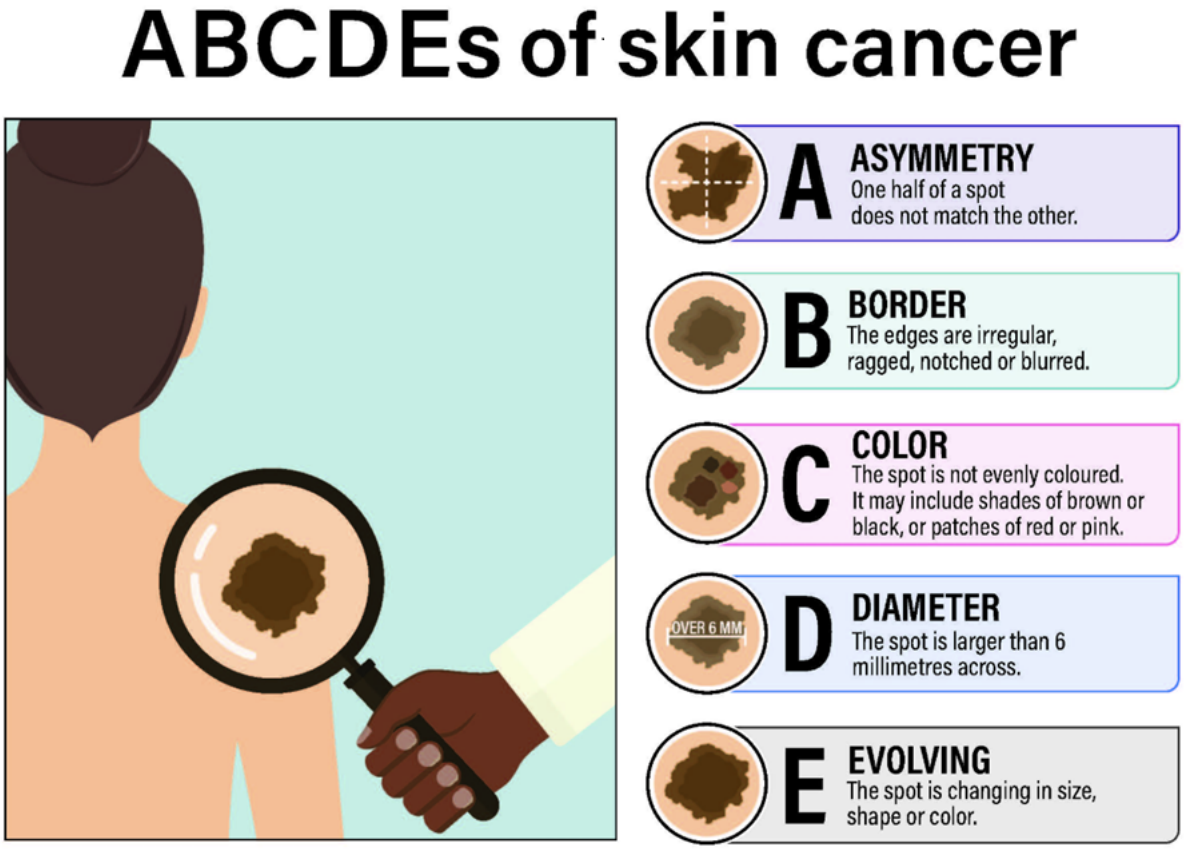


Figure 3. The detection criteria for skin cancer evaluations



DISEASE PATHOLOGY

Skin cancer, like many cancers, is described in stages zero through four (3). Skin cancer begins as a mutated cell, usually due to UV radiation, and if the immune system and tumor suppressing genetics are unable to remove that mutated cell it has the ability to replicate and form a cancerous growth (3). BCC, unlike SCC and melanoma, has no stages due to its relative unlikeliness to spread and is usually a small collection of cancerous cells that can be easily removed (22). However, the first stage, stage 0, of both types, melanoma and SCC, of skin cancer is when the cancer is limited to the top layer of skin and has not moved from the location it developed, at this point the cancer is very low risk and easy to remove (3)(22). After this is stage 1 which is split into stage 1A and 1B (22). In stage 1A the cancer is 10 mm across or smaller and in stage 1B the cancer in inbetween 10mm and 20mm across but has yet to affect supporting tissues (22). Stage 2 is also split into 2A and 2B (22). In stage 2A the cancer is between 10mm and 20 mm and has begun to affect supporting tissues or is between 20mm and 30mm but may or may not have begun to affect supporting tissues (22). Stage 2B has no size associated but the cancer has begun to grow into nearby structures (22). In stage 3 the cancer has reached the nearby lymph nodes but remains localized to one part of the body (22). In Stage 3A the cancer has spread to a lymph node that is on the same side of the body and is 3 cm or smaller (22). In stage 3B the cancer has either spread to a single lymph node on the same side of the body which is larger than 3 cm or it has spread to lymph nodes on the other side of the body (22). Lastly stage 4 indicates that the cancer has spread to another part of the body (22).

Melanoma

There are four main types of melanoma which exist including Superficial spreading melanoma (SSM), Nodular melanoma (NM), Lentigo maligna melanoma (LMM), and Acral lentiginous melanoma (ALM) (24). Other rarer types of melanoma include: Spitz melanoma, Blue nevi melanoma, Congenital melanoma nevi, Nevoid melanoma, Uveal melanoma, Mucosal melanoma, Desmoplastic melanoma (24). SSM is the most common subtype and comprises about 70 percent of cases (24). SSM is linked to intense exposure and is often larger, more asymmetrical and more likely to evolve than the common nevi (24). NM accounts for 15-30 percent of all melanoma cases, though it results in a significantly higher percent of melanoma deaths, showing its relative deadliness (24). NM is usually dome- shaped, polyp like and dark brown or reddish brown but due to its lack of horizontal growth phase it invades the dermis rapidly which leads to quicker metastasis (24). LMM comprises between 4 and 15 percent of melanomas and typically affects areas with high sun exposure (24). It tends to appear as a poorly defined blackish-brown flat lesion that can become raised as the disease progresses (24). Lastly ALM is the rarest of the four accounting only for between 2 and 3 percent of all cases but it is the most common type for those with darker skin tones (24). Unlike other types of melanoma this one is not associated with UV exposure and often appears on lighter skin, like that of the palms or soles (24).

Figure 4. The stages of Melanoma

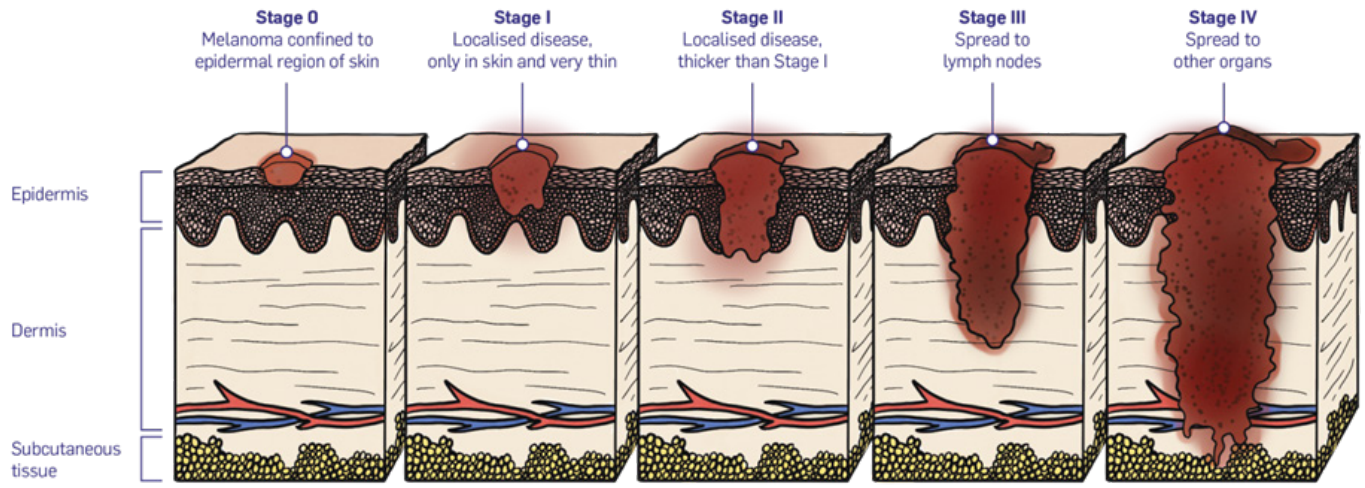
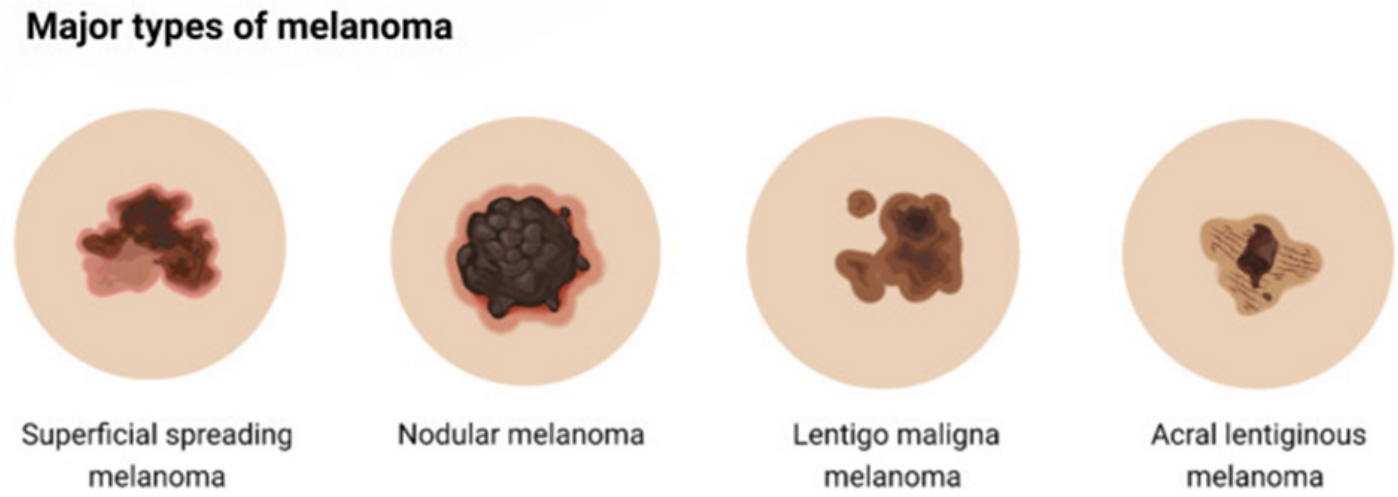


Figure 5. The major types of Melanoma



Basal cell carcinoma

BCC arises from nonkeratinizing cells in the stratum basale and is a less aggressive type of nonmelanoma that is composed of cells similar to the original epidermal basal cells (24). It is further divided into lower risk and higher risk subtypes with the lower risk including nodular BCC, superficial BCC, and pigmented BCC and with higher risk including Micronodular BCC, Morpheaform BCC , Infiltrative BCC, Fibroepithelial BCC (24) Nodular BCC is the most common subtype,comprising about 75% of cases (24) . It is usually pink or skin colored, well defined with rolled edges and visible blood vessels (24). Superficial BCC is a less aggressive, slow-growing form that appears red and scaly allowing it to resemble eczema or psoriasis (24).Pigmented BCC is the variant of nodular BCC more common in individuals with darker skin and appears as a darkly pigmented bump or patch (24).

Micronodular BCC is composed of small, less than 1 mm, dispersed tumor nodules and is more invasive and with higher recurrence rate (24).Morpheaform BCC makes up about 6% of cases and appears as a sunken, scar-like, plaque with a high risk of recurrence and perineural invasion (24). Infiltrative BCC has poorly defined borders which makes it difficult to remove while it also aggressively spreads leading to perineural invasion and high recurrence rates (24). Fibroepithelial BCC contains epithelial and mesenchymal components and has spindle-like cells within the tumor stroma (24).

Squamous cell carcinoma

SCC is the second most prevalent type of Nonmelanoma, accounting for 16 percent of all skin cancers (24). It emerges from epidermal keratinocytes or adnexal compositions in and is associated with long-term exposure to UV radiation (24). SCC is most prominent in areas with high UV exposure like the head and neck which accounts for approximately 55% of all cutaneous SCC (24).

MARKET SIZE

Nonmelanoma accounts for approximately 5.8 percent of all cancer diagnosis, with 1,042,056 new cases annually and melanoma accounts for approximately 1.6 percent of all cancer diagnosis with 287,723 new cases annually (25). Melanoma has the highest rates of incidence in North American countries, mainly the United States and Canada, European countries, mainly northern and western countries, and Australia (26). Global rates of skin cancer are also increasing rapidly, with a 10 percent increase in the last decade according to the WHO (27).

In the United States, skin cancer is the most common cancer with approximately 9,500 people diagnosed with it every day. (29). This number has only risen in recent years with the period of 2000-2010 seeing an increase of BCC and SCC by 145% and 263% respectively (29). Melanoma rates are also increasing with a 31.5 percent increase between 2011 and 2019 and is predicted that in 2025 melanoma will become the 5th most commonly diagnosed cancer in the United States (29). While the current incident rate in the United States for all types of skin cancers is roughly 20 percent, the lifetime incident rate for melanoma is only 3% for people of caucasian descent, .1% for people of african descent, and 0.5 for people of hispanic descent (30). For Asian/Pacific Islanders there is a melanoma incidence of 1.3 per 100,000 and for Native Americans there is an incident rate of 10.7 per 100,000 (29). Melanoma also affects men at a higher rate, accounting for 57.69% of all new cases while women only account for 42.31% of all new cases (29). Age also plays a role in the incidence rate, with the average age of diagnosis for melanoma being 66, though it is one of the most common cancers in young adults especially young women (29).

The global skin cancer market can be broken up into two main sectors, skin cancer treatment and skin cancer diagnostics (31,32). As of 2023, the global treatment market for all major

types of skin cancer is roughly 10.73 billion dollars (31). This is expected to greatly increase to 26.65 billion dollars by 2034 (31). The global skin cancer diagnostic market as of 2023 is 9.1 billion dollars (32). Cumulatively this makes the 2023 skin cancer market worth 19.83 billion USD as of 2023, with a high inclination to increase in the next decade. This increase has been linked to advances in immunotherapy, which have been especially vital in increasing the market size and prognosis for patients with melanoma (33).

Table 1. Skin cancer incidence rate across different continents in 2022 (28).

Continent	Country	Age-standardized rate/ 100,000 people
North America	USA	16.50
South America	Brazil	3.30
Oceania	Australia	37.00
Europe	Italy	12.70
Asia	China	0.37

Figure 6. The incident rates for skin cancer by country and gender

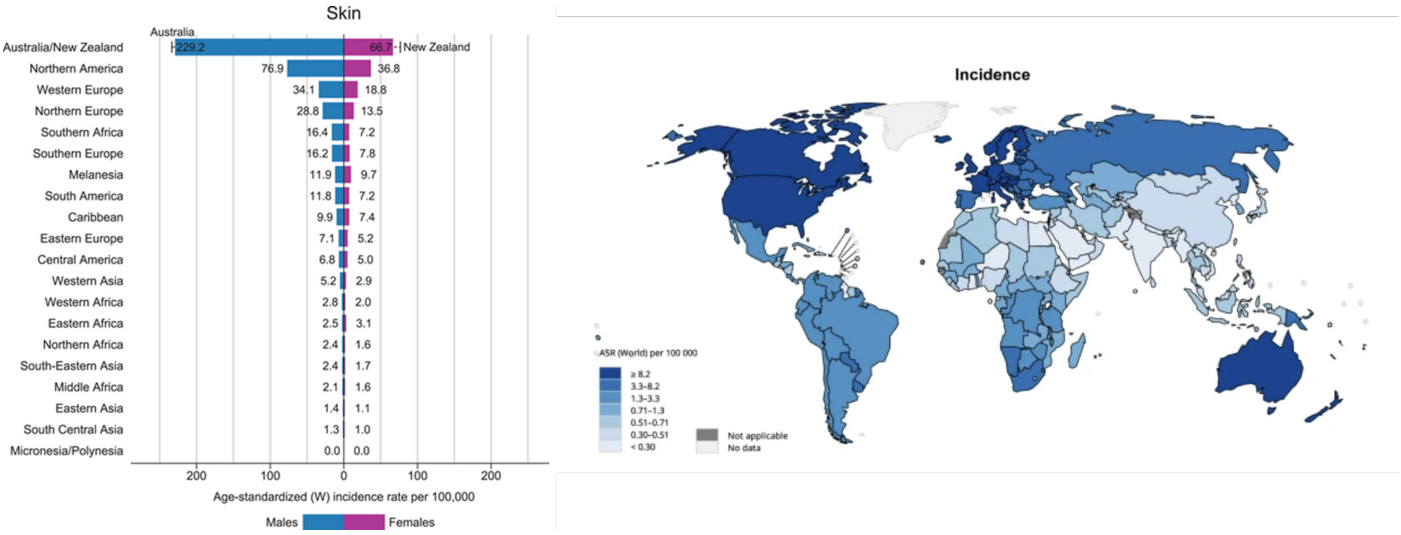
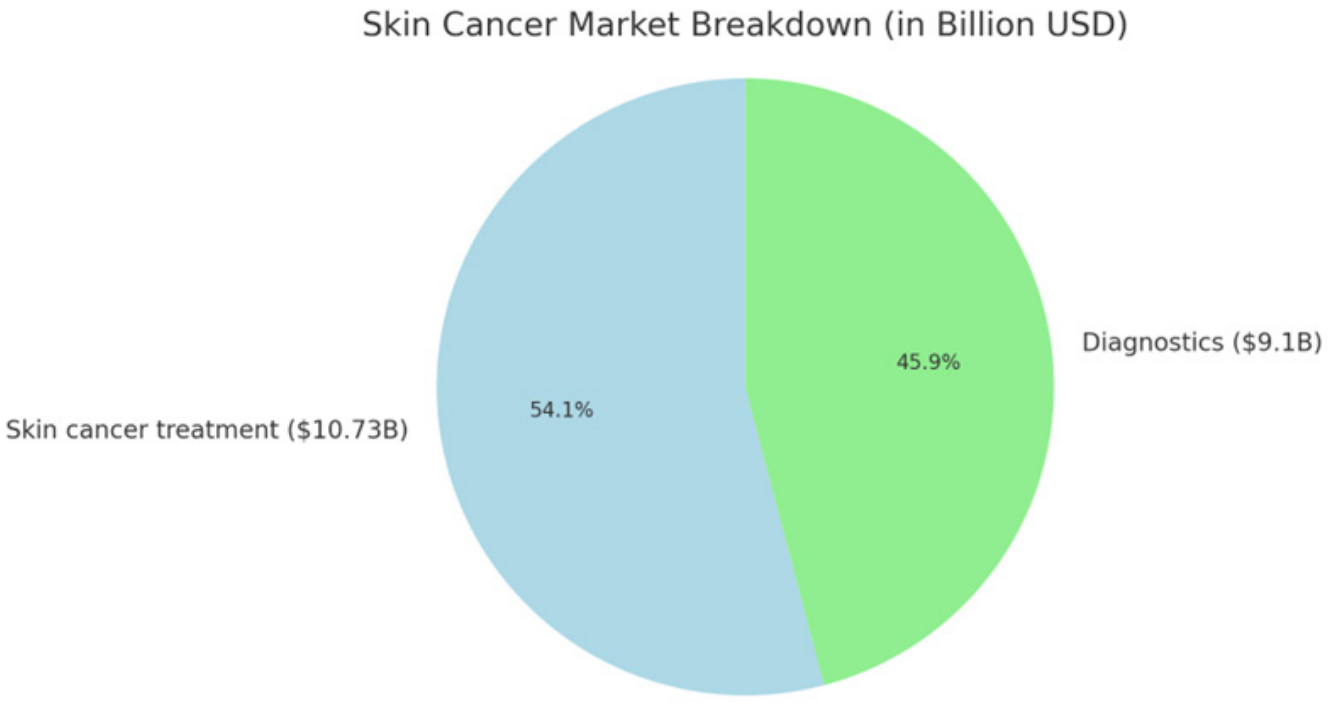


Figure 7. Skin cancer market size



Market Segments and Trends

The market can not only be split between diagnostic and treatment but can be split between the two different types of cancers, melanoma and nonmelanoma and both diagnostics and treatments can be split further (34). The diagnostics market can be split into 4 main categories, skin biopsy, dermatoscopy, diagnostic imaging, and lymph node biopsy (34). In the United States, the total diagnostic skin cancer market was 1.5 billion dollars in 2021, with a split between the four categories favoring skin biopsy and diagnostic imaging (34). The global melanoma diagnostic market is worth 4.6 billion of the total 9.1 billion dollars of cancer diagnosis while the majority of the remaining market value belongs to nonmelanoma cancers like SCC and BCC (35). This market is split between multiple large companies including: Castle Bioscience, DermTech, bioMérieux Inc., Foundation Medicine Inc., DermaSensor, Inc., F Hoffmann-La Roche Ltd, NeoGenomics Laboratories, Quest Diagnostics Incorporated., SkylineDx, and Abbott (32).

The treatment market can also be split by cancers and can be split into types of treatment including therapeutics, and non therapeutic like radiation, and surgical intervention (36). Lower stage treatments are normally linked to non therapeutic treatments, examples of which are presented in Table 2, however as the cancer gets to later stages it is often combined with therapeutics (36). The global therapeutics market for just melanoma was 6.27 billion dollars in 2024 (37). This market can be further divided into the multiple different types of therapeutics which can be seen in figure 8 (38). The market for BCC and SCC treatments was significantly smaller at only 793.4 Million in 2024 (39).

Some of the major players in melanoma treatments, specifically therapeutics include Genentech, Novartis, and Bristol Myers Squibb, Amgen, F. Hoffmann-La Roche Ltd, Merck & Co., Inc., and Sun Pharmaceutical Industries Ltd (33) (40).

Figure 8. Melanoma therapeutics in 2021 and prediction of 2030.

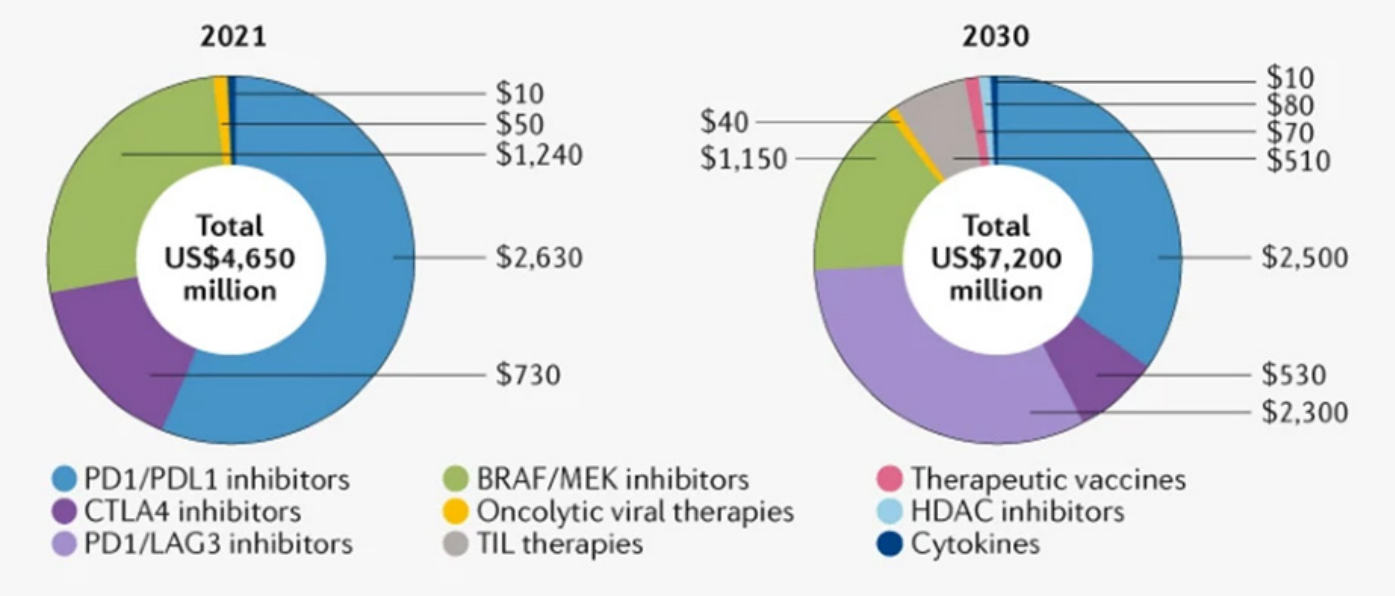


Figure 9. Existing Skin Cancer therapeutics.

Figure 10. The tumor microenvironment causes and repair

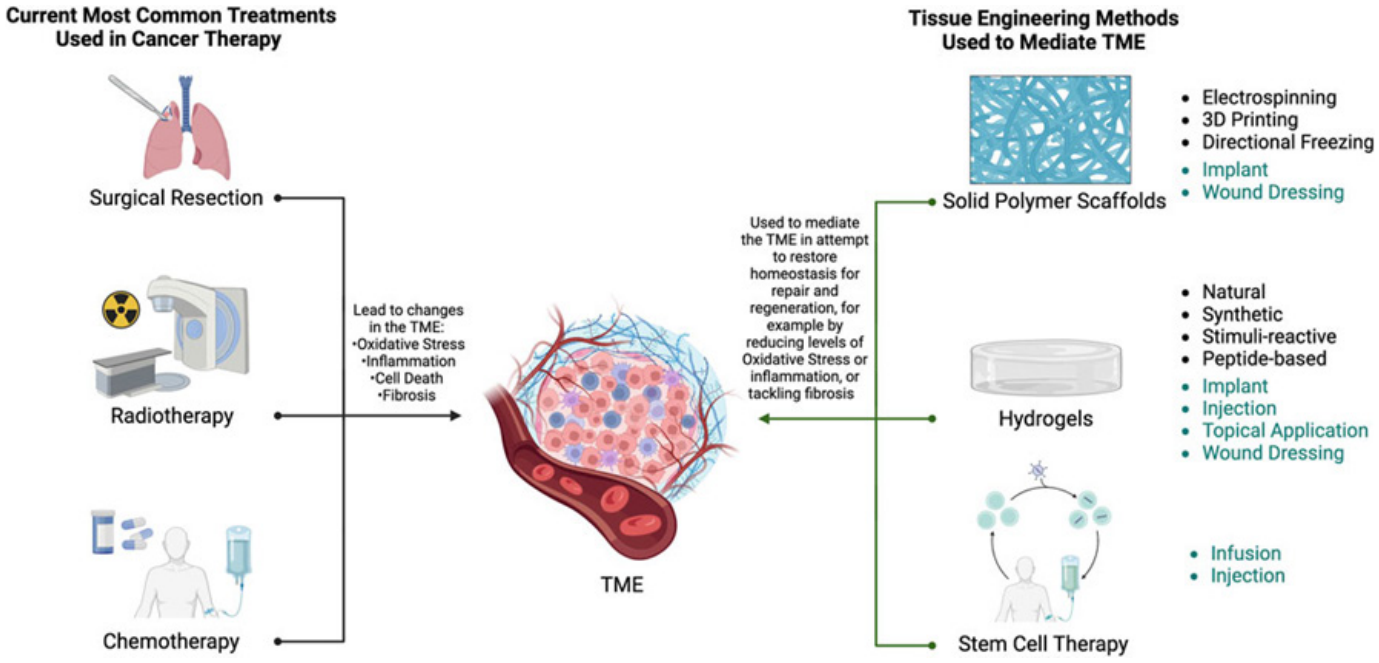
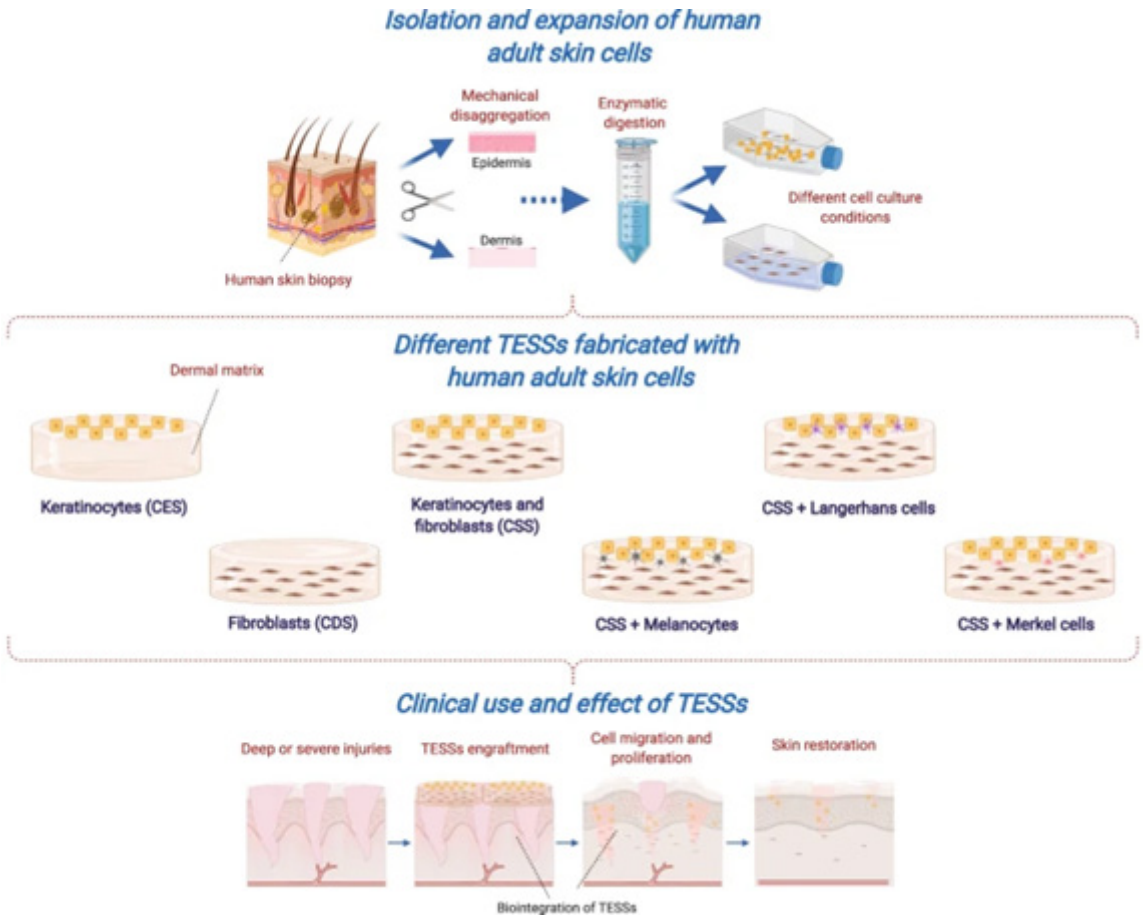


Figure 11. Tissue-engineered skin substitute (TESSs) procedure and clinical usage.



CURRENT PRODUCTS AND PROCEDURES

There are multiple procedures and products that are used to treat BCC, SCC, and melanoma, the majority of which can be found in **Tables 2 and 3** below (36,40).

Table 2. The existing surgical and therapeutic treatment options for the nonmelanoma cancers, BCC and SCC types of skin cancer (36).

Cancer type	Stage of disease	Treatments
Basal cell carcinoma	Localized disease	Surgical excision with margin evaluation
		Mohs micrographic surgery
		Radiation therapy
		Curettage and electrodesiccation
		Cryosurgery
		Photodynamic therapy
		Topical fluorouracil (5-FU)
		Imiquimod topical therapy
		Carbon dioxide laser
	Metastatic or locally advanced disease untreatable by local modalities	Hedgehog pathway inhibitors
	Recurrent nonmetastatic disease	Surgical excision
		Mohs micrographic surgery

Squamous cell carcinoma	Localized disease	Surgical excision with margin evaluation
		Mohs micrographic surgery
		Radiation therapy
		Curettage and electrodesiccation
		Cryosurgery
	Metastatic or locally advanced disease untreatable by local modalities	Immunotherapy (PD-1 inhibitors)
	Recurrent nonmetastatic disease	Surgical excision
		Mohs micrographic surgery
		Radiation therapy

Table 3. The existing surgical and therapeutic treatment options for melanoma skin cancer (41).

Stage of disease	**Treatments**
Stage 0 melanoma	Excision
Stage IA melanoma	Excision +/− sentinel lymph node biopsy
Stage IB melanoma	Excision with lymph node management
Stage II melanoma	Excision with lymph node management
	Adjuvant therapy
Resectable Stage III melanoma	Excision +/− lymph node management
	Neoadjuvant therapy
	Adjuvant therapy
	Combination immunotherapies, including vaccines (under clinical evaluation)
	Adjuvant therapies that target a known pathogenic variant, e.g., KIT (under clinical evaluation)
	Intralesional therapies (under clinical evaluation)
	Immunotherapy
Unresectable Stage III, Stage IV, and Recurrent melanoma	Signal transduction inhibitors
	Intralesional therapy
	Adjunctive local/regional therapy including surgical resection
	Palliative therapy
	Targeted therapy with single agents or combination therapy (under clinical evaluation)
	Combinations of immunotherapy and targeted therapy (under clinical evaluation)
	Intralesional injections (e.g., oncolytic viruses) (under clinical evaluation)
	Complete surgical resection of all known disease versus best medical therapy (under clinical evaluation)
	Isolated limb perfusion for unresectable extremity melanoma (under clinical evaluation)
	Systemic therapy for unresectable disease (under clinical evaluation)

Treatment Drugs

The main drug used for hedgehog therapeutics, the drug therapeutic used for BCC, is called vismodegib, sold as Erivedge® (42). This medication helps disrupt the activity of a group of proteins, hedgehog proteins, which can help shrink large basal cell skin cancers, making surgery more effective (42). This is especially useful for advanced basal cell cancer, since it may keep the tumor in check for months or years (42). The main therapeutic drug used against SCC, PD-1 inhibitors, are monoclonal antibodies that target the PD-1 checkpoint, which keeps T- cells from attacking the body's cells, and boosts the body's immune system against cancerous cells (43). Examples of these PD-1 inhibitors include Pembrolizumab (Keytruda), Nivolumab (Opdivo and Opdivo Qvantig), and Cemiplimab (Libtayo) (43).

Melanoma has three main categories of therapeutic drugs: BRAF inhibitors, MEK inhibitors, and C-KIT inhibitors (47). Since roughly half of all melanomas have mutated BRAF genes which produce altered BRAF proteins that allow them to grow,

by targeting and inhibiting these proteins, these drugs can limit the size of the tumors (47). Examples of BRAF inhibitors include Vemurafenib (Zelboraf), dabrafenib (Tafinlar), and encorafenib (Braftovi). The MEK gene works together with the BRAF gene, so blocking the MEK gene with drugs can also help treat melanomas with BRAF gene changes (47). Examples of MEK inhibitors include trametinib (Mekinist), cobimetinib (Cotellic), and binimetinib (Mektovi) (47). Lastly, a small amount of melanomas, usually acral melanomas or mucosal melanomas, have altered C-KIT genes that help them grow (47). Some C-KIT targeted drugs include imatinib (Gleevec) and nilotinib (Tasigna) (47).

Products in clinical trials

There are multiple clinical trials, and a range of innovative therapies currently being tested to improve the treatment of skin cancers, including both melanoma and non-melanoma types (48). These investigational products span immunotherapy, gene-targeted drugs, engineered tissue substitutes, and novel radiation delivery systems—each with specific objectives aimed at increasing efficacy, safety, and functional outcomes (48).

One major area of focus involves immuno-oncology, such as the Phase 1b study of atezolizumab combined with vemurafenib or vemurafenib plus cobimetinib (49). This trial targets patients with BRAFV600-mutant metastatic melanoma, aiming to evaluate the safety and preliminary efficacy of combining immune checkpoint inhibition with BRAF and MEK inhibitors (49). The goal is to enhance antitumor responses and delay resistance by engaging multiple cancer-fighting mechanisms (49). Similarly, another drug trial investigates Vorinostat, an HDAC inhibitor, in BRAF-mutated melanoma resistant to standard therapies, with the goal of overcoming resistance by modifying gene expression and promoting cancer cell death (50).

Innovative radiation therapies are also being explored, such as Diffusing Alpha-emitter Radiation Therapy (DaRT) (51,52). Two studies evaluate the use of localized alpha radiation emitters for treating malignant skin and superficial soft tissue tumors (51,52). These trials aim to determine the feasibility and tumor-killing effectiveness of this precise, highly cytotoxic approach, which minimizes damage to surrounding healthy tissue compared to traditional radiation methods (51,52).

Additional pharmaceutical approaches are also under investigation, such as the anti-angiogenesis agent AG-013736 for metastatic melanoma, which targets tumor blood supply, and SM-020 Gel, a topical drug under evaluation for treating non-melanoma skin cancers and seborrheic keratoses (53,54). These trials aim to offer less invasive, more tolerable alternatives for managing skin cancer, especially in early or superficial forms (53,54).

The last and very promising category of clinical trials involves tissue-engineered products designed for patients requiring reconstructive surgery after tumor excision (55). For example, the study of an artificial human skin substitute seeks to evaluate its effectiveness in basal cell carcinoma patients undergoing reconstructive procedures (55). This product could significantly improve post-surgical recovery by promoting better integration and regeneration of skin (55). In a related study (NCT02145130), autologous dermal and dermo-epidermal substitutes are being tested for treating skin defects, with goals centered on achieving durable, patient-specific wound coverage that mimics natural skin both functionally and aesthetically (56).

Tissue Engineered and Novel Solutions

In addition to the numerous cancer treatments in clinical trials, there has been academic research which focuses on using tissue engineering principles, like scaffolds, especially hydrogels, as a method of skin cancer treatment (57). Natural, synthetic, and hybrid hydrogels have demonstrated their ability to kill cancer cells, release cancer drugs, which can stop cancer recurrence, and to help with the wound healing process after the cancer has been eradicated (57). The main benefit of these systems, which use existing drugs and chemotherapy, is that unlike their precursors they are highly localized (57). This limits the number of side effects a patient is likely to experience during treatment (57). On top of producing hydrogels, which release drugs into the system after being injected or placed into the patient after surgery, purdue university professor Chi Hwan Lee has created a water soluble patch with silicon microneedles that discarch a high level of anticancer drugs into the wearer (58).

There is also tissue engineering research being done for after skin cancer treatment solutions like mediating the tumor microenvironment and skin substitutes for large skin surgical removals (59,60). The originally surrounding healthy tissue can be damaged during cancer treatment, leading to a harsh microenvironment that can lead to adverse side effects and hinder repair and regeneration of that tissue (59). The surrounding tissues can experience higher levels of reactive oxygen species (ROS), inflammation and cell death and there is evidence that mediating this improves tissue repair and regeneration (59). Electrospun hydrogels made of polymers like PCL or PTFA, have been shown to mimic native ECM to the point that they can create a new microenvironment which is capable of cell attachment, growth, and proliferation (59). Additionally, injectable hydrogels which form a gel in situ creates a non invasive, tissue trauma-limited scaffolds which can release growth factors that create an ECM like structure for cell proliferation (59). If the damage tissue is due to surgical intervention, then tissue-engineered skin substitute (TESSs) which are a combination of autologous culture epithelial substitutes consisting keratinocytes and allogeneic cultured

dermal substitutes which allow for skin cell migration and proliferation into the covered area can be used (60).

CONCLUSIONS

Skin cancer, an incredibly common form of cancer, has three major types: Melanoma, Basal cell carcinoma, and Squamous cell carcinoma all of which are the result of mutations in what used to be healthy skin cells (1,2,3). All three major types of skin cancer have two main market aspects, diagnostics and treatment and collectively all three major skin cancer types diagnostic and treatment markets are roughly 19.8 billion dollars (33). Alongside the very large market is a very large number of existing products for treating both melanoma and the nonmelanoma cancers including chemotherapy, surgery and a number of drugs (36,41). The main drugs used for melanoma include BRAF inhibitors, MEK inhibitors, and C-KIT inhibitors (50). On the other hand the main drugs used for BCC are hedgehog therapeutics and for SCC are PD-1 inhibitors (55,56). There are also numerous products in clinical trials including a Diffusing Alpha-emitter Radiation Therapy (DaRT) device, artificial and autologous human skin substitutes for post surgical use, drugs like anti-angiogenesis agents, combinations of existing BRAF and MEK inhibitors, and new HDAC inhibitors (51-59). Additionally there are novel tissue engineered methods which have yet to reach clinical trials including hydrogels which kill cancer cells, inhibit cancer recurrence, and help with the wound healing process after the cancer has been eradicated (60). These existing and new therapies help contribute to the growing skin cancer market and help to decrease the mortality rate of the common cancer (31,36,41).

Abbreviations

Basal cell carcinoma (BCC), Squamous cell carcinoma (SCC), Ultraviolet (UV), Ultraviolet radiation (UVR), Ultraviolet A (UVA), Ultraviolet B (UVB), Superficial spreading melanoma (SSM), Nodular melanoma (NM), Lentigo maligna melanoma (LMM), Acral lentiginous melanoma (ALM), Reactive Oxygen Species (ROS), Tumor microenvironment (TME), Tissue-engineered skin substitute (TESS),

Funding Sources

There is no funding to report for this study.

Conflict Of Interest

Authors declare that there is no conflict of interest.

Acknowledgements

Sophia Welsh expresses appreciation to Professor Bill Tawil for overseeing the framework of this review, and for the insightful lectures and advice concerning tissue engineering, specifically skin tissue engineering, which contributed to the development of this paper.

Appendix

Companies:

1a. Castle Biosciences: https://castlebiosciences.com/
1b. DermTech: https://dermtech.com/
1c. bioMérieux Inc.: https://www.biomerieux.com/corp/en.html
1d. Foundation Medicine Inc.: https://www.foundationmedicine.com/
1e. DermaSensor, Inc.: https://www.dermasensor.com/
1f. F Hoffmann-La Roche Ltd: https://www.roche.com/
1g. NeoGenomics Laboratories: https://www.neogenomics.com/
1h. Quest Diagnostics Incorporated.: https://www.questdiagnostics.com/
1i. SkylineDx: https://www.skylinedx.com/
1j. Abbott: https://www.abbott.com/
1k. Genentech: https://www.gene.com/
1l. Novartis: https://www.novartis.com/
1m. Bristol Myers Squibb: https://www.bms.com/
1n. Amgen: https://www.amgen.com/
1o. Merck & Co., Inc.: https://www.merck.com/
1p. Sun Pharmaceutical Industries Ltd: https://sunpharma.com/usa/

Products:

2a. Erivedge®: https://www.erivedge.com/
2b. Keytruda®: https://www.keytruda.com/
2c. Opdivo®: https://www.opdivo.com/
2d. Opdivo Qvantig®: https://www.opdivo.com/
2e. Libtayo®: https://www.libtayo.com/
2f. Zelboraf®: https://www.gene.com/patients/medicines/zelboraf
2g. Tafinlar®: https://us.tafinlarmekinist.com/
2h. Braftovi®: https://www.braftovi.com/
2i. Mekinist®: https://us.tafinlarmekinist.com/
2j. Cotellic®: https://www.gene.com/patients/medicines/cotellic
2k. Mektovi®: https://www.pfizer.com/products/product-detail/mektovi
2l. Gleevec®: https://www.oncolink.org/cancer-treatment/oncolink-rx/imatinib-gleevec-R
2m. Tasigna®: https://www.tasigna-hcp.com/

REFERENCES

1. "May Is Skin Cancer Awareness Month." The Skin Cancer Foundation, 29 Apr. 2025, www.skincancer.org/.

2. "Skin Cancer." Mayo Clinic, Mayo Foundation for Medical Education and Research, 8 Apr. 2025, www.mayoclinic.org/diseases-conditions/skin-cancer/symptoms-causes/syc-20377605.

3. "Skin Cancer." Cleveland Clinic, 25 Apr. 2025, my.clevelandclinic.org/health/diseases/15818-skin-cancer.

4. McKnight, Gerard, et al. "Physiology of the skin." Surgery (Oxford), vol. 40, no. 1, Jan. 2022, pp. 8–12, https://doi.org/10.1016/j.mpsur.2021.11.005.

5. Cleveland Clinic medical. "Skin: Layers, Structure and Function." Cleveland Clinic, 19 Mar. 2025, my.clevelandclinic.org/health/body/10978-skin.

6. Lopez-Ojeda, Wilfredo, et al. "Anatomy, Skin (Integument)." StatPearls [Internet]., U.S. National Library of Medicine, 17 Oct. 2022, www.ncbi.nlm.nih.gov/books/NBK441980/.

7. Clayton, Kalum, et al. "Langerhans cells—programmed by the epidermis." Frontiers in Immunology, vol. 8, 29 Nov. 2017, https://doi.org/10.3389/fimmu.2017.01676.

8. "Layers of the Skin." Layers of the Skin | SEER Training, training.seer.cancer.gov/melanoma/anatomy/layers.html. Accessed 13 May 2025.

9. "NCI Dictionary of Cancer Terms." Comprehensive Cancer Information - NCI, www.cancer.gov/publications/dictionaries/cancer-terms/def/merkel-cell. Accessed 13 May 2025.

10. Brown, Thomas M., and Karthik Krishnamurthy. "Histology, Dermis." StatPearls [Internet]., U.S. National Library of Medicine, 14 Nov. 2022, www.ncbi.nlm.nih.gov/books/NBK535346/.

11. "Anatomy and Physiology I." Layers of the Skin | Anatomy and Physiology I, courses.lumenlearning.com/suny-ap1/chapter/layers-of-the-skin/. Accessed 13 May 2025.

12. Jones, Brandi. "What the Hypodermis Layer of the Skin Does." Verywell Health, Verywell Health, 18 Dec. 2024, www.verywellhealth.com/the-hypodermis-is-the-lowermost-layer-of-skin-2710144.

13. Narayanan, Deevya L., et al. "Review: Ultraviolet radiation and skin cancer." International Journal of Dermatology, vol. 49, no. 9, 30 Aug. 2010, pp. 978–986, https://doi.org/10.1111/j.1365-4632.2010.04474.x.

14. Kim, Sang-in, et al. "Formation of cyclobutane pyrimidine dimers at dipyrimidines containing 5-hydroxymethylcytosine." Photochemical & Photobiological Sciences, vol. 12, no. 8, 1 Aug. 2013, pp. 1409–1415, https://doi.org/10.1039/c3pp50037c.

15. Asgari, Maryam M., et al. "Family history of skin cancer is associated with increased risk of cutaneous squamous cell carcinoma." Dermatologic Surgery, vol. 41, no. 4, Apr. 2015, pp. 481–486, https://doi.org/10.1097/dss.0000000000000292.

16. "Non-Melanoma Skin Cancer Risk Factors." Cancer Research UK, 5 Dec. 2024, www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/non-melanoma-skin-cancer/risk-factors.

17. Everett, Jessica. "Genetic Risk Factors for Skin Cancer." Rogel Cancer Center | University of Michigan, 9 Nov. 2022, www.rogelcancercenter.org/living-with-cancer/caregivers-and-family/genetic-risk-factors-skin-cancer.

18. "Melanoma Skin Cancer Risk Factors: Melanoma Risk Factors." Melanoma Skin Cancer Risk Factors | Melanoma Risk Factors | American Cancer Society, www.cancer.org/cancer/types/melanoma-skin-cancer/causes-risks-prevention/risk-factors.html. Accessed 13 May 2025.

19. "Skin Cancer Screening." MD Anderson Cancer Center, www.mdanderson.org/prevention-screening/get-screened/skin-cancer-screening.html. Accessed 13 May 2025.

20. "Study: Skin Cancer among Women with an Inherited BRCA Mutation." Skin Cancer among Women with an Inherited BRCA Mutation, 25 July 2024, www.facingourrisk.org/XRAY/skin-cancer-among-women-with-BRCA-mutations.

21. "Skin Biopsy: Medlineplus Medical Test." MedlinePlus, U.S. National Library of Medicine, medlineplus.gov/lab-tests/skin-biopsy/. Accessed 13 May 2025.

22. "Stages and Grades of Skin Cancer." Stages and Grades | Skin Cancer | Cancer Research UK, 14 Nov. 2024, www.cancerresearchuk.org/about-cancer/skin-cancer/stages-grades.

23. "Stages of Melanoma." MSCAN, 17 Mar. 2025, mscan.org.au/learning-hub/melanoma/stages-of-melanoma/.

24. Roky, Amdad Hossain, et al. "Overview of skin cancer types and prevalence rates across continents." Cancer

Pathogenesis and Therapy, vol. 3, no. 2, Mar. 2025, pp. 89–100, https://doi.org/10.1016/j.cpt.2024.08.002.

25. Bray, Freddie, et al. "Global cancer statistics 2018: Globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries." CA: A Cancer Journal for Clinicians, vol. 68, no. 6, 12 Sept. 2018, pp. 394–424, https://doi.org/10.3322/caac.21492.

26. Huang, Junjie, et al. "Global incidence, mortality, risk factors and trends of melanoma: A systematic analysis of registries." American Journal of Clinical Dermatology, vol. 24, no. 6, 10 June 2023, pp. 965–975, https://doi.org/10.1007/s40257-023-00795-3.

27. "Skin Cancer Market Size, Growth Analysis, Trends Report 2032." Skin Cancer Market Size, Growth Analysis, Trends Report 2032, www.marketresearchfuture.com/reports/skin-cancer-market-1173. Accessed 13 May 2025.

28. "Skin Cancer." American Academy of Dermatology, www.aad.org/media/stats-skin-cancer. Accessed 13 May 2025.

29. "Melanoma Skin Cancer Statistics." Melanoma Skin Cancer Statistics | American Cancer Society, www.cancer.org/cancer/types/melanoma-skin-cancer/about/key-statistics.html#:~:text=Overall%2C%20the%20lifetime%20risk%20of,Factors%20for%20Melanoma%20Skin%20Cancer. Accessed 13 May 2025.

30. Research and Markets. "Skin Cancer Treatment Market Analysis & Forecast 2024-2034: Market by Indication; by Therapy; by Distribution Channel; and by Region." Research and Markets - Market Research Reports - Welcome, www.researchandmarkets.com/reports/5890353/skin-cancer-treatment-market-analysis-and. Accessed 13 May 2025.

31. "Skin Cancer Diagnostics Market Size & Share Report, 2030." Skin Cancer Diagnostics Market Size & Share Report, 2030, www.grandviewresearch.com/industry-analysis/skin-cancer-diagnostics-market-report. Accessed 13 May 2025.

32. "Melanoma Market to Reach USD 8.9 Billion by 2034, Impelled by the Ongoing Advancements in Screening Techniques." BioSpace, 22 July 2024, www.biospace.com/melanoma-market-to-reach-usd-8-9-billion-by-2034-impelled-by-the-ongoing-advancements-in-screening-techniques.

33. U.S. & Canada Skin Cancer Dermatology Market Report, 2022-2030, www.grandviewresearch.com/industry-analysis/us-canada-skin-cancer-dermatology-market. Accessed 13 May 2025.

34. "Melanoma Cancer Diagnostics Market Size & Share: 2034." Fact.MR, Market Research Company, www.factmr.com/report/57/melanoma-cancer-diagnostics-market. Accessed 13 May 2025.

35. Board, PDQ Adult Treatment Editorial. "Skin Cancer Treatment (PDQ®)." PDQ Cancer Information Summaries [Internet]., U.S. National Library of Medicine, 7 Mar. 2025, www.ncbi.nlm.nih.gov/books/NBK65928/.

36. ltd, Research and Markets. "Skin Cancer Drugs Market Report 2025." Skin Cancer Drugs Market Size, Share & Forecast to 2029, www.researchandmarkets.com/report/skin-cancer. Accessed 13 May 2025.

37. Parra, Liseth M., and Rachel M. Webster. "The Malignant Melanoma Market." Nature News, Nature Publishing Group, 27 Apr. 2022, www.nature.com/articles/d41573-022-00075-5.

38. ltd, Research and Markets. "Non-Melanoma Skin Cancer Market Size & Forecast to 2030." Non-Melanoma Skin Cancer Market Size & Forecast to 2030, www.researchandmarkets.com/report/non-melanoma-skin-cancer-drug?srsltid=AfmBOopG6EREvd0e4lV9VOemuDEX5IqoCEitF8DrkRfFeNuwMwPeV_Vk. Accessed 13 May 2025.

39. "Global Skin Cancer Diagnostics and Therapeutics Market Size: Mordor Intelligence." Skin Cancer Diagnostics and Therapeutics Market - Size, Share & Trends, www.mordorintelligence.com/industry-reports/skin-cancer-diagnostics-and-therapeutics-market. Accessed 13 May 2025.

40. Board, PDQ Adult Treatment Editorial. "Melanoma Treatment (PDQ®)." PDQ Cancer Information Summaries [Internet]., U.S. National Library of Medicine, 2 May 2025, www.ncbi.nlm.nih.gov/books/NBK66034/.

41. "Medications for Basal & Squamous Cell Skin Cancers." Patient Care at NYU Langone Health, nyulangone.org/conditions/basal-squamous-cell-skin-cancers/treatments/medications-for-basal-squamous-cell-skin-cancers. Accessed 13 May 2025.

42. "Immune Checkpoint Inhibitors and Their Side Effects."

American Cancer Society, www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy/immune-checkpoint-inhibitors.html. Accessed 13 May 2025.

43. "Collections." National Museum of American History, 13 May 2025, americanhistory.si.edu/collections.

44. "Buy Keytruda (Pembrolizumab) Online • Price & Costs ." Everyone.Org, everyone.org/keytruda-pembrolizumab. Accessed 19 May 2025.

45. "Nice Wants More Information from Roche on Zelboraf." PMLiVE, 5 Feb. 2024, pmlive.com/pharma_news/nice_wants_more_information_from_roche_on_zelboraf_418084/.

46. "Melanoma Targeted Therapy: Targeted Drugs for Melanoma." Melanoma Targeted Therapy | Targeted Drugs for Melanoma | American Cancer Society, www.cancer.org/cancer/types/melanoma-skin-cancer/treating/targeted-therapy.html. Accessed 13 May 2025.

47. Clinicaltrials.Gov, clinicaltrials.gov/search?cond=skin+cancer&intr=drug&page=2. Accessed 13 May 2025.

48. Genentech, Inc. "A Phase 1b Study of Atezolizumab in Combination With Vemurafenib or Vemurafenib Plus Cobimetinib in Participants With BRAFV600-Mutation Positive Metastatic Melanoma." Clinicaltrials.Gov, 21 July 2020, clinicaltrials.gov/study/NCT01656642?cond=skin+cancer&intr=Tissue+engineer&rank=6.

49. The Netherlands Cancer Institute. "HDAC Inhibitor Vorinostat in Resistant BRAF V600 Mutated Advanced Melanoma." Clinicaltrials.Gov, 17 Oct. 2018, clinicaltrials.gov/study/NCT02836548?cond=skin+cancer&intr=drug&page=2&rank=18.

50. Alpha Tau Medical LTD. "Feasibility Trial of Diffusing Alpha-Emitter Radiation Therapy (DaRT) for Malignant Skin & Superficial Soft Tissue Tumors." Clinicaltrials.Gov, 1 June 2022, clinicaltrials.gov/study/NCT04377360?cond=skin+cancer&intr=Tissue+&rank=3.

51. Alpha Tau Medical LTD. "Alpha Radiation Emitters Device (DaRT) for the Treatment of Cutaneous, Mucosal or Superficial Soft Tissue Neoplasia." Clinicaltrials.Gov, 7 Feb. 2025, clinicaltrials.gov/study/NCT04534127?cond=skin+cancer&intr=Tissue+&page=4&rank=36.

52. Pfizer. "Anti-Angiogenesis Agent AG-013736 In Patients With Metastatic Melanoma." Clinicaltrials.Gov, 26 June 2012, clinicaltrials.gov/study/NCT00094107?cond=skin+cancer&intr=drug&rank=1.

53. DermBiont, Inc. "A Trial to Study the Safety and Efficacy of SM-020 Gel 1.0% in Subjects With Seborrheic Keratoses and Non-Melanoma Skin Cancers." Clinicaltrials.Gov, 10 May 2024, clinicaltrials.gov/study/NCT06409195?cond=skin+cancer&intr=drug&rank=7.

54. Andalusian Network for Design and Translation of Advanced Therapies. "Study of an Artificial Human Skin Medicine for Patients With Basal Cell Carcinoma Undergoing Reconstructive Surgery." Clinicaltrials.Gov, 8 Nov. 2023, clinicaltrials.gov/study/NCT05234658?cond=skin+cancer&intr=Tissue+engineer&rank=3.

55. University of Zurich. "Phase I Study for Autologous Dermal Substitutes and Dermo-Epidermal Skin Substitutes for Treatment of Skin Defects." Clinicaltrials.Gov, 8 Sept. 2021, clinicaltrials.gov/study/NCT02145130?cond=skin+cancer&intr=Tissue+&page=2&rank=19.

56. Marzi, Mahrokh, et al. "Hydrogels as promising therapeutic strategy for the treatment of skin cancer." Journal of Molecular Structure, vol. 1262, 6 Apr. 2022, p. 133014, https://doi.org/10.1016/j.molstruc.2022.133014.

57. Service, Purdue News. "Wearable Patch May Provide New Treatment Option for Skin Cancer." Purdue University News, 16 June 2020, www.purdue.edu/newsroom/archive/releases/2020/Q2/wearable-patch-may-provide-new-treatment-option-for-skin-cancer.html.

58. Westwood, Lorna, et al. "The road after cancer: Biomaterials and tissue engineering approaches to mediate the tumor microenvironment post-cancer treatment." Frontiers in Biomaterials Science, vol. 3, 27 Mar. 2024, https://doi.org/10.3389/fbiom.2024.1347324.

59. Sierra-Sánchez, Álvaro, et al. "Cellular human tissue-engineered skin substitutes investigated for deep and difficult to heal injuries." Npj Regenerative Medicine, vol. 6, no. 1, 17 June 2021, https://doi.org/10.1038/s41536-021-00144-0.