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(REVIEW ARTICLE)

The skin's role in immunity

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Abstract

The skin serves as a crucial barrier in the immune system, playing a pivotal role in protecting the body from pathogens. As the largest organ, it provides a physical and chemical barrier against infections while housing various immune cells that contribute to both innate and adaptive immunity. Keratinocytes, the primary cells of the epidermis, produce antimicrobial peptides and cytokines that enhance immune responses. Additionally, specialized immune cells, such as Langerhans cells and dermal dendritic cells, act as sentinels, capturing and presenting antigens to T cells. This interaction initiates immune responses that are essential for long-term protection. Furthermore, the skin's microbiome contributes to immune regulation and homeostasis, influencing inflammatory responses and pathogen resistance. Understanding the skin's multifaceted role in immunity is vital for developing therapeutic strategies against skin-related disorders and systemic diseases. The skin plays a fundamental role in the immune system, acting as the first line of defense against environmental threats, including pathogens, toxins, and physical injuries. As the body's largest organ, it serves both a physical barrier and a dynamic interface for immune responses. The epidermis, composed mainly of keratinocytes, produces antimicrobial peptides (AMPs) and cytokines, which are critical for early immune defense. These substances inhibit microbial growth and initiate inflammatory responses.In addition to keratinocytes, the skin contains specialized immune cells, such as Langerhans cells, dermal dendritic cells, and macrophages. Langerhans cells, located in the epidermis, play a crucial role in antigen presentation, capturing pathogens and migrating to lymph nodes to activate T cells. Dermal dendritic cells complement this function, facilitating the communication between innate and adaptive immunity

Keywords: Skin Immunity; Barrier Function; Immune Cells; Antimicrobial Peptides; Microbiome; Inflammation

1. Introduction

The skin is an essential organ in the immune system, acting as the primary barrier against pathogens while also playing an active role in immune responses. Structurally, the epidermis is equipped with various layers, where keratinocytes form a tough barrier that prevents the entry of harmful microorganisms. Within the epidermis, Langerhans cells function as antigen-presenting cells, detecting invaders and initiating immune responses by migrating to lymph nodes to activate T-cells. The skin also contains other immune cells, such as mast cells and macrophages, which contribute to both innate and adaptive immunity. Additionally, the skin produces a range of antimicrobial peptides (AMPs), such as defensins and catholicising, that directly combat pathogens. Cytokines released by skin cells modulate immune responses, facilitating communication among various immune components. This intricate interplay underscores the skin's dual role as a physical barrier and an active participant in immune surveillance, emphasizing its importance in maintaining overall health and preventing infections.[1]

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1.1. Overview of skin structure

The skin is a complex organ composed of three primary layers: the epidermis, dermis, and hypodermis, each with distinct structures and functions essential for overall health.

- Epidermis: This is the outermost layer, primarily made up of keratinocytes, which produce keratin, a protein that provides strength and waterproofing. The epidermis is also home to melanocytes, responsible for melanin production, which protects against UV radiation, and Langerhans cells, which play a crucial role in the immune response by recognizing and presenting antigens.
- Dermis: Situated beneath the epidermis, the dermis is significantly thicker and contains a dense network of collagen and elastin fibers that provide structural integrity and elasticity. This layer houses essential components such as blood vessels, nerve endings, hair follicles, and various glands, including sweat and sebaceous glands. These structures are vital for thermoregulation, sensory perception, and moisture regulation, enabling the skin to respond to environmental changes effectively.
- Hypodermis: Also known as subcutaneous tissue, this deepest layer consists of loose connective tissue and adipose tissue. It functions primarily as insulation and shock absorption, protecting underlying muscles and bones. The hypodermis also serves as an energy reservoir, storing fat that the body can utilize when needed.[2]

Together, these layers of skin perform crucial functions such as protection against pathogens and physical damage, regulation of body temperature, sensory reception, and synthesis of vitamin D, illustrating the skin's role as a vital organ in maintaining homeostasis and overall health.

1.1.1. Défense Against Pathogens

The immune system identifies and neutralizes foreign invaders. This includes:

Innate Immunity: The first line of defense, which includes physical barriers (skin, mucous membranes) and immune cells that respond quickly to infections.

Adaptive Immunity: A more specific response involving lymphocytes (B and T cells) that recognize specific pathogens and can provide long-term immunity.

1.1.2. Role in Disease Prevention

A well-functioning immune system is essential for preventing diseases. For instance: Vaccinations enhance adaptive immunity by training the immune system to recognize specific pathogens without causing the disease. Immunity is linked to the prevention of various chronic diseases. For example, a compromised immune response can lead to increased susceptibility to infections, cancer, and autoimmune diseases.

1.1.3. Tissue Repair and Recovery

The immune system is integral to healing processes. After an injury or infection, immune cells promote tissue repair and regeneration. This is essential for recovery from both physical injuries and illnesses.

1.1.4. Impact on Mental Health

Recent studies suggest a connection between immune health and mental well-being. Chronic inflammation has been linked to mood disorders, such as depression and anxiety. A healthy immune response may help mitigate these effects.[3]

2. Anatomy of the skin

The skin, the largest organ of the body, serves multiple vital functions, including protection, sensation, and regulation. It consists of three primary layers: the epidermis, dermis, and subcutaneous tissue. The epidermis is the outermost layer, primarily composed of keratinocytes, which produce keratin, a protein that strengthens the skin. This layer also contains melanocytes, responsible for pigmentation, and Langerhans cells, which play a role in immune response. Beneath the epidermis lies the dermis, a thicker layer that contains collagen and elastin fibers, providing structural support and elasticity. This layer houses blood vessels, lymphatic vessels, hair follicles, and sensory receptors, which are crucial for thermoregulation and tactile sensation. Finally, the subcutaneous tissue (or hypodermis) is composed of loose connective tissue and fat cells, which insulate the body and serve as an energy reserve. Overall, the skin not only acts as a barrier against external threats but also participates in homeostasis and sensory perception [4]

2.1. The layers of skin

2.1.1. The Epidermis

The epidermis is the outermost layer of the skin, primarily responsible for protecting underlying tissues and maintaining the body's barrier against environmental factors. It is composed mainly of keratinocytes, which originate from the basal layer and undergo a process of keratinization as they move upward through the strata of the epidermis. This layer consists of five distinct sub-layers: the stratum corneum (outermost), stratum lucidum (found only in thick skin), stratum granulosum, stratum spinosum, and stratum basale (innermost).

The stratum corneum consists of dead, flattened keratinocytes that form a tough, protective layer, while the stratum basale contains actively dividing cells, including melanocytes, which produce melanin that contributes to skin color and protects against UV radiation. The epidermiis avascular, relying on diffusion from the underlying dermis for nutrients and waste removal, and is essential for water retention and overall skin integrity.[5]

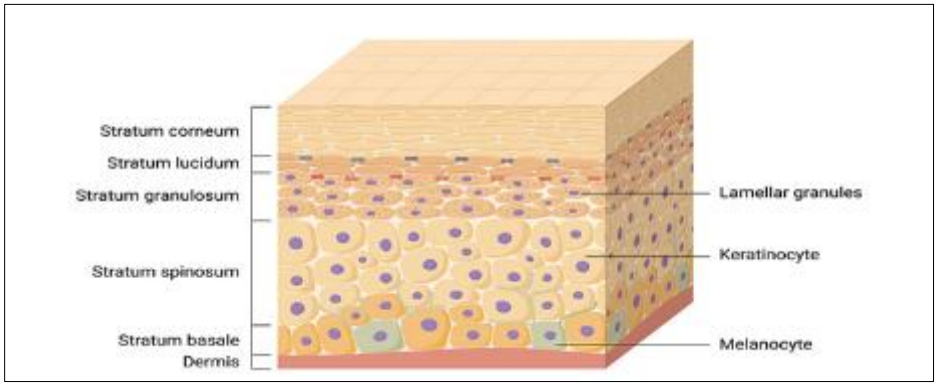

Figure 1 Epidermis [5]

2.1.2. The Dermis

The dermis is the middle layer of the skin, situated between the epidermis and the subcutaneous tissue, and is significantly thicker than the epidermis. It is composed primarily of dense connective tissue, which provides structural support, strength, and elasticity due to the presence of collagen and elastin fibers. The dermis is divided into two regions: the papillary dermis, which contains thin, finger-like projections that interdigitate with the epidermis, enhancing nutrient exchange and sensation, and the reticular dermis, which is denser and houses larger blood vessels, nerve endings, hair follicles, and sebaceous and sweat glands. These components play critical roles in thermoregulation, sensation, and the overall function of the skin. Additionally, the dermis contains specialized cells such as fibroblasts, which produce collagen and elastin, and immune cells that help protect against pathogens.[6]

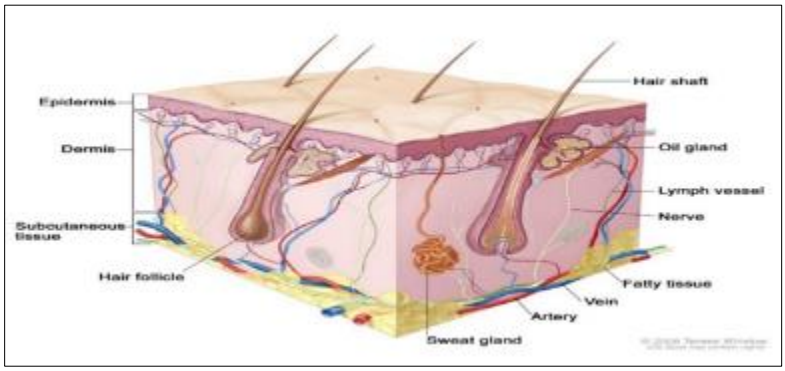

Figure 2 Dermis [6]

2.1.3. The Hypodermis

The hypodermis, also known as the subcutaneous layer, is the deepest layer of the skin, lying beneath the dermis. It primarily consists of loose connective tissue and adipose tissue, which serve several important functions. This layer acts as an insulator, helping to regulate body temperature by minimizing heat loss, and it provides cushioning and protection for underlying muscles and bones. The adipose tissue within the hypodermis also serves as an energy reservoir, storing fat that the body can utilize during times of energy deficit. Additionally, the hypodermis contains larger blood vessels and nerves that branch into the dermis and epidermis, facilitating communication and nutrient supply to the upper skin layers. Its flexible structure allows the skin to move freely over underlying tissues without restriction. Overall, the hypoderm plays a critical role in thermoregulation, shock absorption, and energy storage, contributing significantly to the overall health and functionality of the skin.[7]

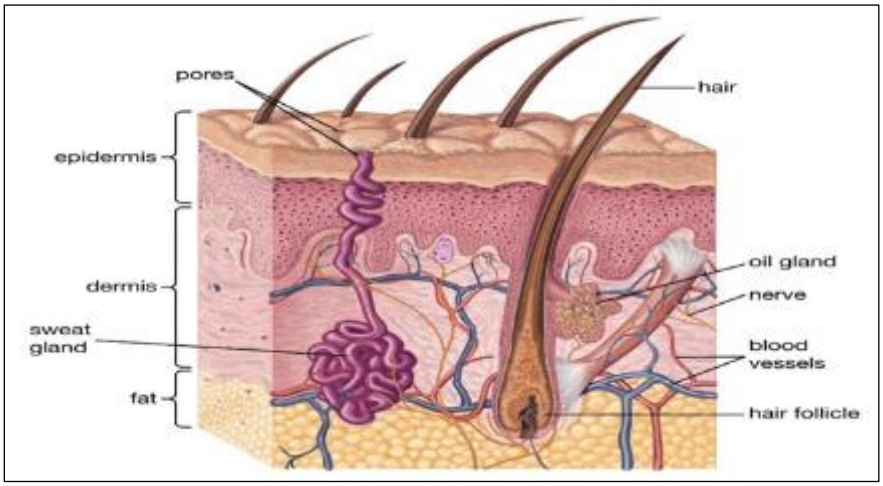

Figure 3 The Hypodermis [7]

3. The skin as a barrier

3.1. Physical Barrier Properties of the Skin

The skin's physical barrier properties are essential for protecting the body from environmental hazards while maintaining homeostasis. Key features of this barrier include:

3.1.1. Stratum Corneum Structure

- The outermost layer of the epidermis, the stratum corneum, is primarily composed of dead keratinocytes, known as corneocytes, which are embedded in a lipid-rich matrix. This structure provides a formidable barrier against water loss and the entry of pathogens. The intercellular lipids, including ceramides, cholesterol, and free fatty acids, create a lamellar structure that enhances barrier integrity and hydration.

3.1.2. Keratinization Process

- Keratinocytes undergo a process called keratinization, where they differentiate and produce keratin, a tough fibrous protein. As these cells migrate from the basal layer to the surface, they lose their nuclei and cytoplasmic contents, becoming flattened and hardened. This process not only strengthens the barrier but also helps to prevent mechanical damage and desiccation.

3.1.3. Water Retention and Hydration

- The skin barrier is critical for preventing transepidermal water loss (TEWL). The lipids in the stratum corneum play a crucial role in retaining moisture and keeping the skin hydrated. An intact barrier prevents excessive moisture loss, which is vital for maintaining skin elasticity and function.

3.1.4. Immunological Defense

- While primarily a physical barrier, the skin also serves as an immunological first line of defense. Langerhans cells, present in the epidermis, play a role in immune surveillance by detecting and presenting antigens to the immune system. This function complements the physical barrier by providing an adaptive immune response against potential threats.

3.1.5. Mechanical Resilience

- The skin is inherently resilient due to its layered structure, which can absorb and dissipate mechanical forces. This property protects underlying tissues from injury and supports overall body movement.[8]

3.2. Role of Skin pH

3.2.1. Acid Mantle

- The skin's surface is covered by an acid mantle, which has a slightly acidic pH ranging from 4.5 to 5.5. This acidic environment is created by the secretion of sebum and sweat.

3.2.2. Barrier Function:

- Microbial Défense: The low pH helps inhibit the growth of pathogenic bacteria and fungi while promoting the growth of beneficial microorganisms (skin microbiome). This balance is essential for preventing infections and maintaining skin health.

3.2.3. Enzyme Activity:

- Lipase and Protease Function: The acid pH is optimal for enzymes that break down lipids and proteins, aiding in the natural exfoliation process and maintaining skin hydration.

3.2.4. Skin Conditions

- Impact on Disorders: An imbalance in skin pH can lead to various skin conditions.
- Alkaline Skin: An increase in pH (making the skin more alkaline) can disrupt the acid mantle, leading to dryness, irritation, and increased susceptibility to infections and dermatitis.
- Acidic Skin: A persistently low pH can contribute to conditions like eczema or acne by encouraging inflammatory responses [9]

3.3. Role of Moisture

3.3.1. Hydration and Barrier Function

- Stratum Corneum Hydration: The outermost layer of the skin, the stratum corneum, relies on moisture to maintain its structure and function. Proper hydration helps keratinocytes remain flexible, which is crucial for the barrier's integrity.
- Transepidermal Water Loss (TEWL): Moisture helps minimize TEWL, the process through which water evaporates from the skin surface. Excessive TEWL can lead to dryness, irritation, and compromised barrier function.[10]

3.3.2. Natural Moisturizing Factors (NMFs):

- Composition: The stratum corneum contains natural moisturizing factors, such as amino acids, urea, and lactate, that attract and bind water, helping to keepthe skin hydrated.
- Role in Skin Elasticity: Adequate moisture levels contribute to the skin’s elasticity and suppleness, reducing the appearance of fine lines and wrinkles.

3.3.3. pH and Moisture Interrelationship:

- Synergistic Effects: The skin's pH and moisture levels are interrelated. A balanced pH promotes effective moisture retention through the action of NMFs and the integrity of the lipid barrier.

- Emollients and Humectants: Skincare products often contain emollients (which soften and smooth the skin) and humectants (which attract moisture). These compounds can help maintain both pH and moisture balance.

3.3.4. Skin Conditions:

- Dry Skin (Xerosis): Conditions that lead to low moisture levels can exacerbate dryness, resulting in scaling, itching, and increased susceptibility to irritants and allergens.

- Eczema and Psoriasis: These conditions are often characterized by disrupted moisture levels and pH imbalance, leading to inflammation and skin barrier dysfunction.[11]

4. Skin diseases and immune response

Skin diseases encompass a wide range of conditions that affect the skin's structure and function, often leading to significant physical and psychological impacts. Below is a detailed overview of several common skin diseases, their causes, symptoms, and treatment options

4.1. Eczema (Atopic Dermatitis)

- Description: Eczema is a chronic inflammatory skin condition characterized by dry, itchy, and inflamed skin. It often starts in childhood and can persist into adulthood.
- Causes: The exact cause is multifactorial, involving genetic predisposition, environmental factors, and immune dysregulation.
- Symptoms: Common symptoms include dry skin, intense itching, red or brownish-gray patches, and thickened, cracked skin.
- Treatment: Management typically includes moisturizers, topical corticosteroids, and, in severe cases, systemic medications like immunosuppressants or biologics.[12]

4.2. Psoriasis

- Description: Psoriasis is an autoimmune condition that accelerates skin cell turnover, leading to the formation of thick, scaly patches.
- Causes: The etiology is related to genetic factors, immune system dysfunction, and environmental triggers such as stress and infections.
- Symptoms: It manifests as red patches covered with thick, silvery scales, often found on the elbows, knees, scalp, and lower back. Patients may also experience itching and pain.
- Treatment: Treatment options include topical treatments (corticosteroids, vitamin D analogs), phototherapy, and systemic therapies such as methotrexate, cyclosporine, and biologics.[13]

4.3. Acne Vulgaris

- Description: Acne is a common skin condition that occurs when hair follicles become clogged with oil and dead skin cells, leading to inflammation.
- Causes: Factors contributing to acne include hormonal changes, bacterial overgrowth (particularly Propionibacterium acnes), and increased sebum production.
- Symptoms: Characterized by the presence of comedones (blackheads and whiteheads), papules, pustules, and sometimes cysts.
- Treatment: Treatment options range from topical retinoids and benzoyl peroxide to systemic antibiotics and hormonal therapies. Severe cases may require isotretinoin.[14]

4.4. Dermatitis

- Description: Dermatitis is an umbrella term for inflammation of the skin, with various types including contact dermatitis, seborrheic dermatitis, and stasis dermatitis.
- Causes: Causes vary widely and include allergens, irritants, and underlying health conditions.
- Symptoms: Symptoms often include red, itchy rashes, swelling, and sometimes blistering.

- Treatment: Management focuses on avoiding triggers, using topical corticosteroids, and employing emollients to soothe the skin.[15]

4.5. Skin Cancer

- Description: Skin cancer is the abnormal growth of skin cells, commonly due to UV radiation exposure. The main types include basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and melanoma.
- Causes: UV radiation from the sun or tanning beds is a major risk factor, along with genetic predisposition.
- Symptoms: Symptoms vary by type but may include new growths, changes in existing moles, or sores that do not heal.
- Treatment: Treatment options include surgical excision, radiation therapy, and, in the case of melanoma, targeted therapies and immunotherapy.[16]

5. Age related changes in skin immunity

Age-related changes in skin immunity significantly affect the skin's ability to respond to pathogens, heal wounds, and maintain overall homeostasis. These changes are attributed to intrinsic factors associated with aging and extrinsic factors such as environmental exposure.

5.1. Decreased Immune Cell Function

As individuals age, there is a notable decline in the function of various immune cells within the skin:

- Langerhans Cells: These dendritic cells in the epidermis are crucial for antigen presentation and initiating immune responses. Studies show a reduction in the number and function of Langerhans cells in older adults, leading to diminished capacity to detect and respond to antigens.

- T Cells: Aging affects both the number and functionality of T cells, particularly CD4+ T helper cells and CD8+ cytotoxic T cells. This decline can lead to reduced immune surveillance and a slower response to infections.[17]

5.2. Altered Cytokine Production

The production of cytokines, which are crucial for cell signaling in immune responses, also changes with age:

- Pro-inflammatory Cytokines: Older adults often exhibit an increased baseline level of pro-inflammatory cytokines (a phenomenon known as "inflammaging"), which can contribute to chronic inflammation and an increased risk of skin disorders.

- Reduced Anti-inflammatory Responses: The capacity to produce anti-inflammatory cytokines like IL-10 decreases, leading to an imbalance that may exacerbate inflammatory skin conditions such as eczema and psoriasis.[18]

5.3. Impaired Skin Barrier Function

Aging leads to structural changes in the skin that compromise its barrier function:

- Decreased Lipid Production: The production of lipids in the stratum corneum diminishes with age, which is essential for maintaining skin hydration and barrier integrity. A compromised barrier can increase susceptibility to infections and irritants.
- Thinner Epidermis: The epidermis thins with age, which can impair the skin’s physical barrier and reduce its capacity to initiate immune responses effectively.[19]

5.4. Reduced Wound Healing

- The ability to heal wounds declines with age due to both intrinsic and extrinsic factors: Slower Inflammatory Response: The inflammatory phase of wound healing is prolonged in older adults, delaying the overall healing process.
- Decreased Growth Factor Production: Age-related reductions in growth factors such as epidermal growth factor (EGF) and fibroblast growth factor (FGF) hinder the proliferation and migration of keratinocytes and fibroblasts, critical for skin repair. [20]

5.5. Increased Susceptibility to Skin Diseases

Aging skin becomes more susceptible to various dermatological conditions:

- Skin Cancers: The cumulative effects of UV exposure and immune senescence contribute to an increased risk of skin cancers, such as basal cell carcinoma and melanoma.
- Chronic Conditions: Conditions like chronic dermatitis, infections, and autoimmune diseases become more prevalent in older populations due to weakened skin immunity.
- Description: Cutaneous lupus erythematosus is a manifestation of systemic lupus erythematosus (SLE) that primarily affects the skin.
- Pathophysiology: This autoimmune condition involves a complex interplay of genetic, environmental, and hormonal factors, leading to the production of autoantibodies and immune complex deposition in the skin.
- Symptoms: The most common skin manifestations include a butterfly-shaped rash across the cheeks and nose, discoid lesions, and photosensitivity. Lesions can be erythematous and scaly.
- Treatment: Treatment often includes topical corticosteroids and antimalarials such as hydroxychloroquine. In severe cases, systemic corticosteroids and immunosuppressive agents may be necessary.[21]

5.6. Vitiligo

- Description: Vitiligo is an autoimmune disorder characterized by the loss of skin pigmentation due to the destruction of melanocytes.
- Pathophysiology: The immune system mistakenly targets melanocytes, leading to their destruction. Genetic predisposition and environmental triggers, such as sunburn or stress, can initiate or exacerbate the condition.
- Symptoms: It presents as white patches on the skin, which can vary in size and distribution. The condition may also affect hair and mucous membranes.
- Treatment: Treatments include topical corticosteroids, calcineurin inhibitors, and phototherapy. For some patients, depigmentation of surrounding skin or skin grafting may be considered.[22]

5.7. Contact Dermatitis

- Description: Contact dermatitis is an inflammatory skin condition resulting from exposure to allergens or irritants.
- Pathophysiology: It is mediated by immune responses, particularly delayed-type hypersensitivity reactions involving T cells. Allergic contact dermatitis occurs when a sensitized individual encounters a specific allergen, while irritant contact dermatitis results from direct damage to the skin barrier.
- Symptoms: Symptoms include redness, swelling, itching, and the formation of blisters or rash in the affected areas.
- Treatment: Management involves identifying and avoiding the irritant or allergen, topical corticosteroids, and in severe cases, systemic corticosteroids or immunosuppressants.[23]

5.8. Implications For Skin Health in Older Adults

The skin undergoes numerous changes with aging, significantly impacting its health and function. Understanding these implications is crucial for maintaining skin integrity and overall well-being in older adults.

5.8.1. Structural Changes

- Aging Skin: The skin experiences a decrease in collagen and elastin, leading to reduced elasticity and firmness. The epidermis thins, which compromises the skin barrier and increases vulnerability to injuries and infections.
- Implications: Thinner skin is more prone to bruising, tearing, and the formation of chronic wounds. This makes older adults more susceptible to skin injuries and complicates healing processes.[24]

5.8.2. Decreased Barrier Function

- Barrier Integrity: The stratum corneum's lipid content decreases with age, impairing moisture retention and making the skin more susceptible to irritants and pathogens.
- Implications: A compromised barrier can lead to conditions such as eczema, dermatitis, and increased risk of infections. Proper skin hydration becomes essential to maintain barrier function and prevent skin conditions.[25]

5.8.3. Altered Immune Function

- Immune Response: The skin's immune response diminishes with age due to a decrease in Langerhans cells and T-cell function, contributing to a phenomenon known as "inflammaging".
- Implications: Older adults are at a higher risk for infections and may have a delayed response to vaccines. This requires careful monitoring and potentially more aggressive preventive measures against infections.[26]

5.8.4. Increased Risk of Skin Diseases

- Common Conditions: Aging skin is more susceptible to a variety of dermatological conditions, including skin cancers (e.g., basal cell carcinoma, squamous cell carcinoma), psoriasis, and chronic dermatitis.
- Implication: Regular dermatological check-ups become critical for early detection and management of these conditions. Educating older adults about sun protection and skin cancer awareness is vital for prevention [27]

5.8.5. Changes in Sensation

- Sensory Decline: Aging can diminish the number of nerve endings in the skin, leading to reduced sensitivity to touch, pain, and temperature
- Implications: Reduced sensation can delay the detection of injuries and increase the risk of burns and other injuries, as older adults may not respond to harmful stimuli effectively [28]

5.8.6. Psychosocial Factors

- Impact on Quality of Life: Skin conditions can significantly affect the psychological well-being of older adults. Issues such as eczema, psoriasis, and skin cancer can lead to feelings of embarrassment, anxiety, and depression
- Implications: Mental health support and counseling should be integrated into the management of skin disorders to address the emotional and psychological impacts of skin health on older adults [29]

6. Future reasearch and therapeutic approaches

Recent innovations in dermatology related to skin immunity focus on understanding the skin's immune system, developing targeted therapies, and utilizing advanced technologies for skin health. Here are several key advancements:

6.1. Innovations in dermatology related to skin immunity

6.1.1. Microbiome Research

- Overview: The skin microbiome plays a crucial role in immune function. Innovations in understanding how microbial diversity affects skin immunity have led to new therapeutic strategies.
- Topical Probiotics: Research shows that applying probiotics can help restore balance to the skin microbiome, enhancing skin barrier function and reducing inflammation in conditions like eczema and acne.
- Prebiotics: Compounds that promote the growth of beneficial skin bacteria are being developed to improve skin health and immune responses.[30]

6.1.2. Biologic Therapies

- Overview: Biologics are targeted therapies designed to modulate the immune system in chronic inflammatory skin diseases.
- Dupilumab: This monoclonal antibody inhibits interleukin-4 and interleukin-13 signaling, providing effective treatment for atopic dermatitis by enhancing skin immunity and reducing inflammation.
- Other Targeted Therapies: New biologics targeting specific pathways in psoriasis and other inflammatory skin diseases are under development, offering treatment options [31]

6.1.3. Immunomodulatory Agents

- Overview: Topical immunomodulators are being used to treat various skin conditions by directly affecting immune responses.
- Tacrolimus and Pimecrolimus: These calcineurin inhibitors are effective in treating eczema and are used to modulate T-cell activation and inflammatory.
- Innovative Delivery Systems: Advances in nanotechnology are improving the delivery of these agents, enhancing their efficacy and reducing systemic side effects. [32]

6.1.4. Gene Therapy

- Overview: Gene therapy approaches are being explored to treat genetic skin disorders and enhance skin immunity.
- CRISPR/Cas9: This technology is being investigated for its potential to correct genetic defects that impair skin immune function, offering hope for conditions like epidermolysis bullosa.
- Gene Editing for Psoriasis: Targeting specific genes involved in inflammatory pathways could lead to new treatments for psoriasis by resetting the immune response.[33]

6.1.5. Artificial Intelligence (AI) in Dermatology

- Overview: AI technologies are improving the diagnosis and management of skin conditions, enhancing understanding of skin immunity.
- Predictive Analytics: AI algorithms analyze patient data to predict flare-ups in conditions like eczema or psoriasis, allowing for proactive management.
- Tele dermatology: Remote monitoring and AI-based assessment can help track skin health and immune responses over time, facilitating timely interventions.[34]

Figure 4 Artificial Intelligence (AI) in Dermatology [33]

6.2. Potential therapies targeting skin immune response

Targeting the skin immune response has become a promising area of research for treating various dermatological conditions, particularly inflammatory diseases and skin cancers. Here are some potential therapies being explored:

6.2.1. Biologic Therapies

- Overview: Biologics are engineered proteins that specifically target components of the immune system.
- IL-23 and IL-17 Inhibitors: Drugs like guselkumab (IL-23 inhibitor) and secukinumab (IL-17 inhibitor) have shown efficacy in treating psoriasis by modulating the immune response and reducing inflammation These therapies target specific cytokines involved in the inflammatory cascade.
- Dupilumab: This monoclonal antibody blocks the IL-4 receptor, effectively treating atopic dermatitis by reducing Th2-mediated inflammation. Clinical trials have demonstrated significant improvements in symptoms and skin clearance.[31]

6.2.2. Topical Immunomodulators

- Overview: These agents modulate immune responses in the skin and are particularly useful for conditions like eczema and psoriasis.
- Calcineurin Inhibitors: Tacrolimus and pimecrolimus are non-steroidal medications that inhibit T-cell activation and reduce inflammation without the side effects associated with long-term steroid use.
- New Formulations: Innovations in formulation, such as microneedle delivery systems, are being developed to enhance the penetration and effectiveness of these drugs in the skin.[35]

6.2.3. Small Molecule Therapies

- Overview: Small molecules can interfere with specific immune pathways.
- JAK Inhibitors: Janus kinase (JAK) inhibitors, such as tofacitinib and baricitinib, have shown promise in treating atopic dermatitis and psoriasis by blocking intracellular signaling pathways involved in inflammation. These inhibitors prevent the activation of immune cells and the release of pro-inflammatory cytokines.
- Phosphodiesterase-4 (PDE4) Inhibitors: Apremilast is a PDE4 inhibitor that reduces inflammation in psoriasis by modulating multiple cytokine pathways.[36]

6.2.4. Gene Therapy

- Overview: Gene therapy offers a novel approach by directly modifying the genetic factors influencing skin immunity.
- CRISPR/Cas9 Technology: This gene-editing tool is being explored to correct mutations associated with skin disorders, enhancing the skin's immune response. Applications include targeted correction of genes involved in inflammatory pathways or skin barrier function.[33]

6.2.5. Vaccination Strategies

- Overview: Therapeutic vaccines aim to stimulate the immune system against specific skin diseases.
- Cancer Vaccines: Research into vaccines for melanoma and other skin cancers is underway, utilizing tumor antigens to elicit a strong immune response against malignant cells.
- Infection Prevention: Vaccines aimed at preventing skin infections, such as those caused by Staphylococcus aureus, are being studied to enhance skin immunity and prevent related complications.[37]

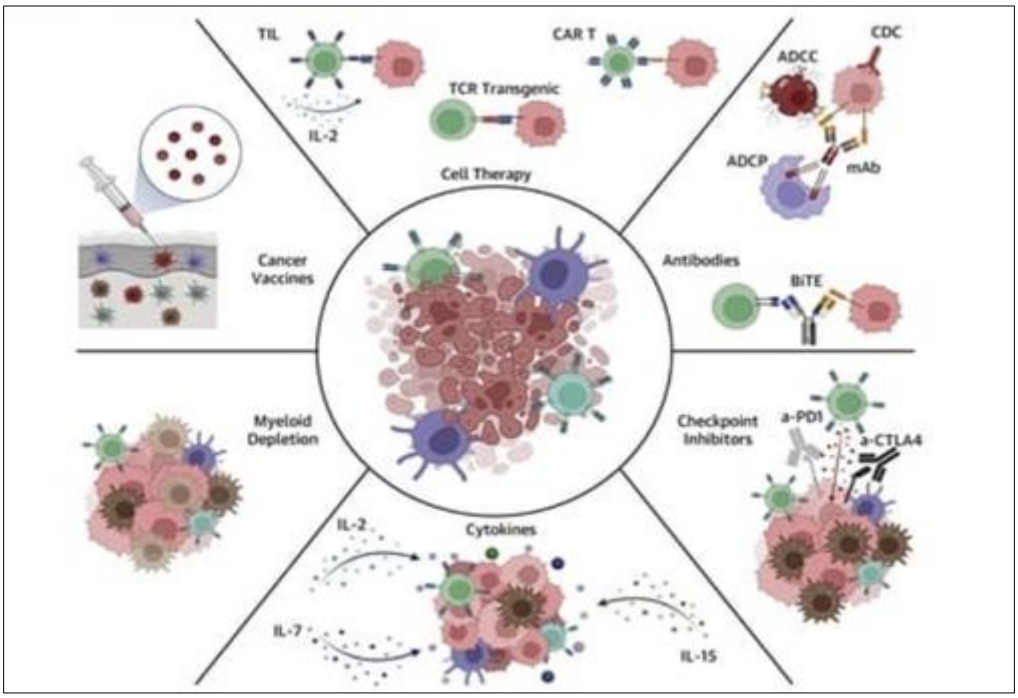

Figure 5 Potential therapies targeting skin immune response [37]

7. Conclusion

The microbiota of the skin affects inflammatory reactions and pathogen resistance while also aiding in immune modulation and homeostasis. Developing treatment plans for systemic illnesses and skin-related conditions requires an understanding of the skin's complex function in immunity.

Compliance with ethical standards

Disclosure of conflict of interest

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