

Molecular Genetics of Skin Pigmentation Disorders: Vitiligo, Albinism, and Melasma

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Abstract

Human skin pigmentation arises from precisely regulated interactions between melanocyte development, melanogenic activity, and melanin transfer within the epidermis. Alterations in these processes lead to a broad range of pigmentary disorders that present as either reduced or excessive pigmentation. Vitiligo, albinism, and melasma represent three major pigmentation disorders with distinct clinical presentations and molecular etiologies, offering critical insight into melanocyte biology and its regulatory networks. This review synthesizes current knowledge on the molecular genetic mechanisms governing these conditions, with particular focus on genes, signaling pathways, and cellular processes involved in melanocyte survival, differentiation, and melanin synthesis. Vitiligo is discussed as a multifactorial autoimmune disorder characterized by genetically driven immune dysregulation, oxidative stress, and targeted destruction of melanocytes. Albinism is examined as a group of inherited disorders in which melanocyte numbers remain preserved, but melanin production is impaired due to mutations affecting melanogenic enzymes and melanosomal structure or function. Melasma is reviewed as an acquired hyperpigmentation disorder marked by enhanced melanocyte activity, influenced by hormonal signaling, ultraviolet radiation, genetic susceptibility, and epigenetic regulation. Comparative analysis of these disorders highlights how disruptions at distinct stages of pigment biology result in divergent phenotypic outcomes. Advances in molecular genetics and pigment cell research have redefined pigmentation disorders as mechanistically driven diseases, providing a foundation for the development of targeted, personalized, and mechanism-based therapeutic approaches.

Keywords

Skin pigmentation; Melanocyte biology; Melanogenesis; Vitiligo; Albinism; Melasma; Molecular genetics; Immune-mediated depigmentation; Oxidative stress; Epigenetic regulation

I. Introduction

The process of human skin pigmentation is complex and strictly controlled, and it is essential for thermoregulation, photoprotection, and individual identification. The makeup and distribution, and composition of melanin, a pigment made by skin cells called melanocytes, are the main factors involved in skin colour variation among human tones. These cells move to the basal layer of the epidermis, hair follicles, and other tissues that contain pigment after rising from the neural crest during embryogenesis (Lin and Fisher, 2007; Yamaguchi and Hearing, 2009). Specific variations in skin pigmentation result from differences in melanogenic activity, melanosome size, number, and transfer efficiency to keratinocytes rather than variation in melanocyte number itself, even though melanocyte density is generally have cross ethnic groups.

By absorbing and dispersing damaging wavelengths, melanin serves as the main endogenous defensive mechanism against UV radiation, reducing UV-induced DNA damage, oxidative stress, and photocarcinogenesis (Cichorek et al., 2013). Human skin produces two main types of melanin: pheomelanin, a red-yellow pigment that shows less UV protection and may increase oxidative stress when exposed to UV light, and eumelanin, a brown-black pigment with potent photoprotective properties (Ito and Wakamatsu, 2008). Visible skin colour and sensitivity to UV-related skin illnesses are determined by the relative amount of these pigments, melanosome shape, and degradation dynamics.

An integrated network of genetic, enzymatic, and signaling mechanisms controls melanin creation, also known as melanogenesis, which takes place within special lysosome-related organelles called melanosomes. Tyrosine is sequentially converted into melanin by the enzymes tyrosinase (TYR), tyrosinase-related protein-1 (TYRP1), and tyrosinase-related protein-2 (TYRP2/DCT), which are essential to melanogenesis (Hearing, 2011). Microphthalmia-associated transcription factor (MITF), a master regulator necessary for melanocyte development, survival, differentiation, and pigment synthesis, is principally responsible for the transcriptional regulation of these melanogenic enzymes (Levy et al., 2006). Melanocortin-1 receptor (MC1R), Wnt/ β -catenin, stem cell factor (SCF)/KIT, endothelin, and cyclic AMP-dependent signaling are just a few of the pathways from which MITF integrates upstream signals. It enables melanocytes to react constantly to environmental triggers such as UV radiation and hormonal stimulation (Busca and Ballotti, 2000; Slominski et al., 2012).

Skin diseases, which can show up as hypo- or hyperpigmentation of the skin, hair, and eyes, are caused by disruption of these highly controlled molecular pathways. Clinically diverse, pigmentary disorders might be acquired or congenital, regional or widespread, temporary or permanent. Melasma, vitiligo, and albinism are the three main types of pigmentation disorders among these illnesses, each with a unique molecular pathophysiology and etiology. When taken as a whole, these conditions offer useful models for comprehending immunological control, melanocyte biology, and gene-environment interactions related to human pigmentation.

Vitiligo is a frequently acquired depigmenting illness that presents as well-defined depigmented patches and granules due to the selective loss of melanocytes. Vitiligo, which affects 0.5–2% of people worldwide, can develop at any age and is often linked to a substantial psychological and social cost (Taïeb and Picardo, 2009). A complex etiology involving intrinsic melanocyte abnormalities, autoimmune processes, oxidative stress, and hereditary vulnerability is supported by current findings. Numerous susceptibility loci linked to immunological modulation, antigen presentation, and melanocyte survival have been found by genome-wide association studies, confirming vitiligo as a complex polygenic illness (Jin et al., 2012; Spritz, 2013). Vitiligo is classified as a classic

autoimmune skin disease because melanocyte death is primarily caused by cytotoxic CD8⁺ T cells, interferon- γ signaling, and chemokine-mediated immune responses. (Rashighi and Harris, 2017).

On the other hand, problems in melanin production, rather than melanocyte loss, are the primary cause of albinism, a diverse collection of inherited hypopigmentation illnesses. In addition to ocular problems such as nystagmus, decreased visual acuity, photophobia, and aberrant optic nerve decussation, people with albinism usually have generalized hypopigmentation of the skin and hair from birth (Grønskov et al., 2007). Mutations in genes producing melanogenic enzymes, melanosomal transporters, or proteins involved in melanosome biosynthesis and maturation cause albinism at the molecular level. Despite having a normal amount of melanocytes, some genetic abnormalities diminish or eliminate pigmentation by impairing melanin formation (Kausar et al., 2018). Clarifying the genetic and cellular processes controlling melanogenesis and melanosome dynamics has been made possible by studies of albinism.

Melasma presents as an acquired disorder of hyperpigmentation, manifesting as symmetric brown or gray-brown macules that predominantly affect sun-exposed facial areas. The condition disproportionately impacts women and individuals with darker skin phototypes (Fitzpatrick types III–VI). Its etiology is multifactorial, strongly driven by hormonal fluctuations—such as those seen in pregnancy or with oral contraceptive use and exacerbated by chronic ultraviolet (UV) exposure (Grimes, 2009).

Distinct from depigmenting disorders like vitiligo or albinism, which involve the loss of melanocytes or enzymatic deficiencies, melasma is a disorder of hyperfunction. It is defined by melanocytic hyperactivity and upregulated melanin synthesis. This dysregulation stems from altered crosstalk between melanocytes, keratinocytes, fibroblasts, and the dermal microenvironment (Kang et al., 2010). Furthermore, genetic predisposition is a critical factor, evidenced by frequent familial clustering. The persistence and recurrence of the disease are driven by a complex interplay of dysregulated estrogen receptors, melanocortin signaling, inflammatory mediators, and various growth factors (Passeron and Picardo, 2018).

Achieving a comprehensive grasp of the molecular genetics governing pigmentation is pivotal for precise diagnosis, prognosis, and therapeutic innovation. Recent breakthroughs in genomics, molecular dermatology, and pigment cell biology have reframed pigmentary disorders: they are no longer viewed merely as cosmetic issues but as well-defined molecular pathologies. By elucidating the specific genetic and signaling pathways driving melanocyte dysfunction, researchers have identified novel therapeutic targets. This progress is currently paving the way for mechanism-based, personalized treatment strategies (Ezzedine et al., 2015; Pillaiyar et al., 2017).

In this review, we critically examine the molecular and genetic mechanisms underpinning vitiligo, albinism, and melasma. We place specific emphasis on the key genes, signaling pathways, and pathogenic processes responsible for melanocyte dysfunction and melanin dysregulation. By synthesizing current molecular evidence, this article aims to establish a comprehensive framework for understanding pigmentation disorders, while highlighting emerging avenues for future research and targeted therapeutic interventions.

II. Biology of Skin Pigmentation

Human skin color is the visible outcome of tightly coordinated biological processes involving melanocyte development, melanin synthesis, and regulated pigment distribution within the epidermis. Melanocytes arise from multipotent neural crest cells during embryogenesis and migrate along defined dorsolateral pathways before localizing primarily to the basal layer of the epidermis and hair follicles. Following migration, these precursor cells differentiate into mature melanocytes capable of producing melanin (Thomas and Erickson, 2008). The accuracy of this developmental sequence—migration, survival, and differentiation—is fundamental to normal pigmentation, and disruption at any stage predisposes to pigmentary abnormalities.

Melanin production occurs within melanosomes, specialized lysosome-related organelles unique to melanocytes. Melanosome biogenesis is a highly ordered process consisting of four progressive stages, beginning with structurally immature premelanosomes and culminating in fully melanized organelles that are transferred to surrounding keratinocytes via dendritic extensions (Raposo and Marks, 2007). This transfer is essential,

as keratinocytes ultimately determine visible skin color by the amount, type, and distribution of melanin they receive.

The biochemical pathway governing pigment synthesis, collectively termed melanogenesis, is initiated from the amino acid tyrosine. Tyrosinase (TYR) serves as the rate-limiting enzyme, catalyzing the hydroxylation of tyrosine to dihydroxyphenylalanine (DOPA) and the subsequent oxidation to dopaquinone. Downstream regulation is mediated by tyrosinase-related proteins TYRP1 and TYRP2 (dopachrometautomerase), which modulate pigment stability and influence the qualitative nature of melanin produced (Hearing, 2011). Variations in enzymatic activity, substrate availability, and intracellular redox balance determine whether melanogenesis favors eumelanin, a brown–black pigment with strong photoprotective capacity, or pheomelanin, a red–yellow pigment associated with reduced ultraviolet (UV) protection (Ito and Wakamatsu, 2008).

At the molecular level, melanocyte identity and melanogenic competence are governed by microphthalmia-associated transcription factor (MITF), which functions as the master transcriptional regulator of melanocyte biology. MITF directly controls the expression of genes involved in melanocyte survival, melanosome formation, and melanin synthesis, including TYR, TYRP1, and TYRP2 (Levy et al., 2006). Even subtle alterations in MITF expression or activity can therefore produce marked effects on pigmentation.

Melanocyte function is further shaped by extracellular signaling pathways that converge on MITF regulation. The melanocortin-1 receptor (MC1R)–cyclic adenosine monophosphate (cAMP) pathway plays a central role in UV-induced pigmentation responses. Activation of MC1R elevates intracellular cAMP levels, enhances MITF transcriptional activity, and promotes eumelanin synthesis, thereby increasing photoprotection (Busca and Ballotti, 2000). The Wnt/ β -catenin pathway is essential during embryonic melanocyte specification and remains important for maintaining melanocyte homeostasis in adult skin (Yamaguchi et al., 2008). In parallel, stem cell factor (SCF) signaling through the KIT receptor supports melanocyte survival and migration, while endothelin signaling contributes to melanocyte proliferation and resistance to apoptosis (Slominski et al., 2012).

Disruption of these tightly regulated processes—whether through inherited mutations, epigenetic changes, or environmental influences—can impair melanocyte function and

melanin production. Reduced melanocyte number or defective melanogenesis results in hypopigmentation disorders, such as vitiligo and albinism, whereas sustained activation of melanogenic pathways underlies hyperpigmentation conditions such as melasma. Thus, skin pigmentation reflects a finely balanced biological system, and disturbances in melanocyte development, enzymatic machinery, or regulatory signaling form the molecular basis of diverse pigmentary disorders discussed in subsequent sections. The molecular regulation of melanogenesis and pigment distribution is summarized in Figure 1

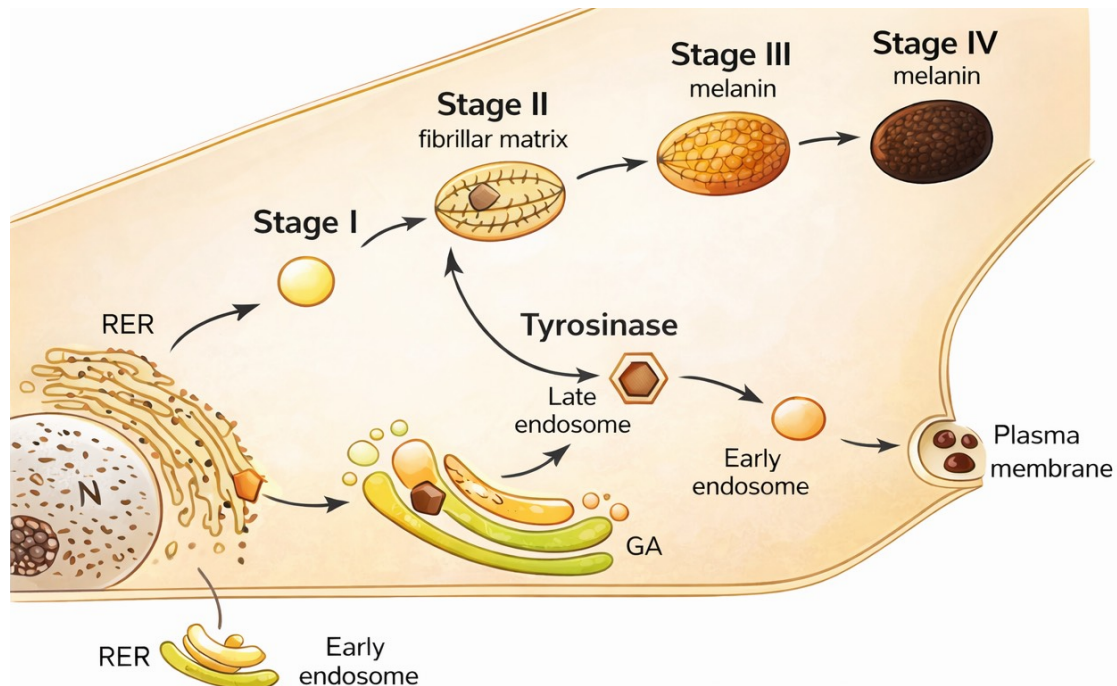


Figure 1. Melanosome maturation and melanogenesis in melanocytes (adapted from Research Gate)

Melanin is produced inside specialized organelles called melanosomes, which mature through four stages from early vesicles to fully pigmented structures. This process is driven by the enzyme tyrosinase and related proteins, leading to the formation of mature melanin that is later transferred to surrounding skin cells.

III. Molecular Genetics of Vitiligo

Vitiligo is a chronic, acquired depigmenting disorder characterized by the progressive development of sharply demarcated depigmented macules and patches resulting from the selective loss of functional melanocytes. The condition affects approximately 0.5–2% of the global population and occurs across all ethnic

groups and geographic regions. Accumulating evidence indicates that vitiligo is a multifactorial disease arising from the interplay between genetic susceptibility, immune dysregulation, oxidative stress, and environmental triggers. Among these contributing factors, molecular genetic studies have firmly established vitiligo as a complex autoimmune disorder with a strong heritable component (Taïeb and Picardo, 2009; Spritz, 2013).

Genome-wide association studies (GWAS) have played a pivotal role in uncovering the genetic architecture of vitiligo. These large-scale analyses have identified numerous susceptibility loci, many of which encode proteins involved in immune regulation, antigen processing, and melanocyte biology. The enrichment of immune-related genes

among vitiligo risk loci highlights the central role of immune-mediated mechanisms, while the involvement of melanocyte-specific genes underscores the intrinsic vulnerability of melanocytes in affected individuals (Jin et al., 2012). Unlike classical pigmentary disorders caused by single-gene defects, vitiligo exhibits a polygenic inheritance pattern, with multiple genetic variants each contributing incrementally to disease risk.

Several immune-related genes have been consistently implicated in vitiligo pathogenesis. The NLRP1 gene is a key component of innate immune signaling and regulates inflammasome activation, leading to the production of pro-inflammatory cytokines such as interleukin-1 β (IL-1 β). Genetic variants in NLRP1 are believed to enhance inflammatory signaling, thereby creating a microenvironment that favours melanocyte injury and immune activation (Levandowski et al., 2013). Another well-established susceptibility gene, PTPN22, encodes a protein tyrosine phosphatase that plays a critical role in T-cell receptor signaling and immune tolerance. Polymorphisms in PTPN22 are associated with several autoimmune diseases, including vitiligo, and are thought to promote aberrant activation of autoreactive T cells (Spritz, 2013).

Genes involved in antigen presentation also contribute significantly to disease susceptibility. Variants within the major histocompatibility complex (MHC), particularly those affecting HLA-DRB1, influence the efficiency with which melanocyte-derived antigens are presented to the immune system. Enhanced antigen presentation increases the likelihood of activating autoreactive T cells, ultimately leading to targeted melanocyte destruction (Jin et al., 2010). In parallel, melanocyte-specific genes such as TYR, which encodes the melanogenic enzyme tyrosinase, have been identified as vitiligo-associated loci. Tyrosinase functions not only as a key enzyme in melanin synthesis but also as a prominent autoantigen, thereby providing a direct molecular link between melanocyte physiology and immune recognition (Spritz et al., 2010).

Oxidative stress represents another critical component of vitiligo pathogenesis and interacts closely with genetic and immune factors. Melanocytes from vitiligo patients exhibit heightened sensitivity to oxidative damage due to increased levels of reactive oxygen species (ROS) and compromised antioxidant defense systems. Excessive ROS accumulation can induce melanocyte apoptosis and promote the release of

damage-associated molecular patterns, which further stimulate innate immune responses and amplify local inflammation (Schallreuter et al., 2008). Oxidative stress is therefore considered an early initiating event that may precede and exacerbate autoimmune-mediated melanocyte destruction.

Both innate and adaptive immune responses are actively involved in the progression of vitiligo. Innate immune activation, particularly through inflammasome signaling pathways, contributes to cytokine release and local inflammatory responses within the skin. The adaptive immune response is predominantly mediated by cytotoxic CD8⁺ T cells that recognize melanocyte antigens and induce melanocyte apoptosis through perforin- and granzyme-dependent mechanisms (Rashighi and Harris, 2017). Interferon- γ signaling and its downstream chemokine network play a crucial role in recruiting, activating, and sustaining these autoreactive T cells in lesional skin, thereby perpetuating disease activity.

In summary, the molecular genetics of vitiligo reveal a complex pathogenic framework involving polygenic susceptibility, immune dysregulation, and oxidative stress-induced melanocyte vulnerability. The convergence of innate and adaptive immune pathways supports the classification of vitiligo as a systemic autoimmune disorder rather than a purely localized skin disease. Elucidating these genetic and molecular mechanisms has not only advanced our understanding of vitiligo pathogenesis but has also paved the way for the development of targeted immunomodulatory therapies and precision-based treatment strategies.

IV. Molecular Genetics of Albinism

Albinism represents a group of inherited pigmentary disorders characterized by a partial or complete reduction in melanin synthesis affecting the skin, hair, and eyes. Unlike vitiligo, melanocytes are present in normal numbers in individuals with albinism; however, defects in melanin biosynthesis or melanosome function prevent adequate pigment production. Clinically, albinism is broadly categorized into oculocutaneous albinism (OCA), involving the skin, hair, and eyes, and ocular albinism, which primarily affects ocular tissues with minimal or absent cutaneous involvement (Grønskov et al., 2007). These conditions are present from birth and display marked phenotypic variability depending on the underlying genetic defect.

At the molecular level, albinism arises from mutations in genes essential for melanogenesis and melanosome integrity. One of the most frequently affected genes is *TYR*, which encodes tyrosinase, the rate-limiting enzyme in melanin synthesis. Pathogenic variants in *TYR* lead to reduced or absent tyrosinase activity, resulting in diminished melanin production. The severity of pigmentation loss depends on whether mutations cause complete enzymatic inactivity or partial functional impairment (Kausar et al., 2018). Mutations in *TYR* account for one of the most prevalent forms of oculocutaneous albinism worldwide.

Several additional genes contribute to the genetic heterogeneity of albinism. The *OCA2* gene encodes a melanosomal membrane protein involved in regulating melanosomal pH and maintaining optimal conditions for tyrosinase activity. *TYRP1* participates in melanin polymerization and stabilization, while *SLC45A2* and *SLC24A5* encode solute carrier proteins required for ion transport and melanosome maturation. Disruption of these pathways interferes with melanosome structure, trafficking, and enzymatic efficiency, ultimately impairing pigment synthesis (Montoliu et al., 2014). These findings underscore the importance of coordinated melanosomal function for normal pigmentation.

Most forms of albinism follow an autosomal recessive inheritance pattern, requiring pathogenic variants in both alleles for disease manifestation. In addition to cutaneous hypopigmentation, individuals with albinism commonly exhibit ocular abnormalities such as nystagmus, photophobia, reduced visual acuity, and abnormal retinal development. These visual defects arise from insufficient melanin production in the retinal pigment epithelium during embryogenesis, which disrupts normal optic nerve decussation and visual pathway development (Grønskov et al., 2007).

Recent advances in molecular diagnostics, particularly next-generation sequencing (NGS), have substantially improved the identification of causative mutations and the classification of albinism subtypes. Molecular diagnosis facilitates accurate genetic counseling, carrier detection, and prenatal testing, thereby enhancing patient management and enabling early visual rehabilitation strategies.

V. Molecular Genetics of Melasma

Melasma is a common acquired hyperpigmentation disorder characterized by

symmetric brown to gray-brown macules, predominantly affecting sun-exposed areas of the face. The condition occurs more frequently in women and individuals with darker skin phototypes and is strongly associated with hormonal influences, pregnancy, oral contraceptive use, and chronic ultraviolet (UV) radiation exposure. Unlike vitiligo and albinism, melasma is not a monogenic disorder but rather a polygenic and multifactorial condition driven by the interaction of genetic susceptibility, environmental exposure, and hormonal signaling (Grimes, 2009).

At the molecular level, melasma is characterized by increased melanocyte activity rather than an increase in melanocyte number. Gene expression studies have demonstrated upregulation of key melanogenic regulators, including *MC1R*, *TYR*, and *MITF*, within lesional skin. Enhanced activity of these genes promotes increased melanin synthesis and augmented transfer of melanosomes to keratinocytes, resulting in visible hyperpigmentation (Passeron and Picardo, 2018).

Hormonal regulation plays a central role in melasma pathogenesis. Estrogen receptors are overexpressed in melasma-affected skin, and estrogen signaling has been shown to stimulate melanocyte activity and melanogenesis. This molecular mechanism provides a plausible explanation for the strong female predominance and the frequent onset or exacerbation of melasma during pregnancy and hormonal therapy.

Vascular alterations also contribute to disease pathophysiology. Increased expression of vascular endothelial growth factor (VEGF) has been observed in melasma lesions, leading to enhanced dermal vascularization. This vascular component may indirectly promote melanocyte hyperactivity by increasing the local availability of growth factors, oxygen, and inflammatory mediators (Kang et al., 2010).

Epigenetic regulation has emerged as an important contributor to melasma. Altered DNA methylation patterns and dysregulated microRNA expression affecting melanocyte signaling and inflammatory pathways have been reported, suggesting that melasma-associated gene expression changes are dynamic and influenced by environmental exposure (Zhang et al., 2019). UV radiation acts as a major triggering factor by inducing oxidative stress, stimulating melanocyte activity, and promoting dermal extracellular matrix remodeling, thereby contributing to the chronic and recurrent nature of the disorder.

VI. Comparative Molecular Mechanisms

Vitiligo, albinism, and melasma share a common biological foundation involving melanocyte function and melanogenesis; however, they differ fundamentally in their underlying molecular mechanisms. Vitiligo is defined by the progressive loss of melanocytes, albinism results from inherited defects in melanin synthesis or melanosome function, and melasma is characterized by melanocyte hyperactivity and excessive melanin production. These distinctions illustrate how perturbations at different stages of pigment biology can produce clinically distinct outcomes.

Melanogenesis represents a shared pathway affected across all three disorders. In albinism, mutations in melanogenic enzymes or melanosomal transport proteins directly impair melanin synthesis despite the presence of melanocytes. In vitiligo, melanogenesis is secondarily disrupted due to immune-mediated melanocyte destruction, whereas in melasma, melanogenic pathways are upregulated, resulting in increased melanin production and deposition (Passeron and Picardo, 2018).

Oxidative stress is another overlapping mechanism with disorder-specific roles. In vitiligo, oxidative stress functions as a critical initiating and amplifying factor that promotes melanocyte apoptosis and immune activation. In melasma, UV-induced oxidative stress enhances melanocyte stimulation and dermal remodeling, while in albinism oxidative stress does not represent a primary pathogenic driver.

Immune dysregulation is a defining feature unique to vitiligo. Both innate and adaptive immune responses contribute to disease pathogenesis, with inflammasome activation, cytokine release, and cytotoxic CD8 T-cell-mediated melanocyte destruction playing central roles (Rashighi and Harris, 2017). In contrast, immune involvement is minimal in albinism and melasma, which are primarily driven by enzymatic, hormonal, vascular, and epigenetic mechanisms. A comparative overview of these pathogenic mechanisms is illustrated in Figure 2.

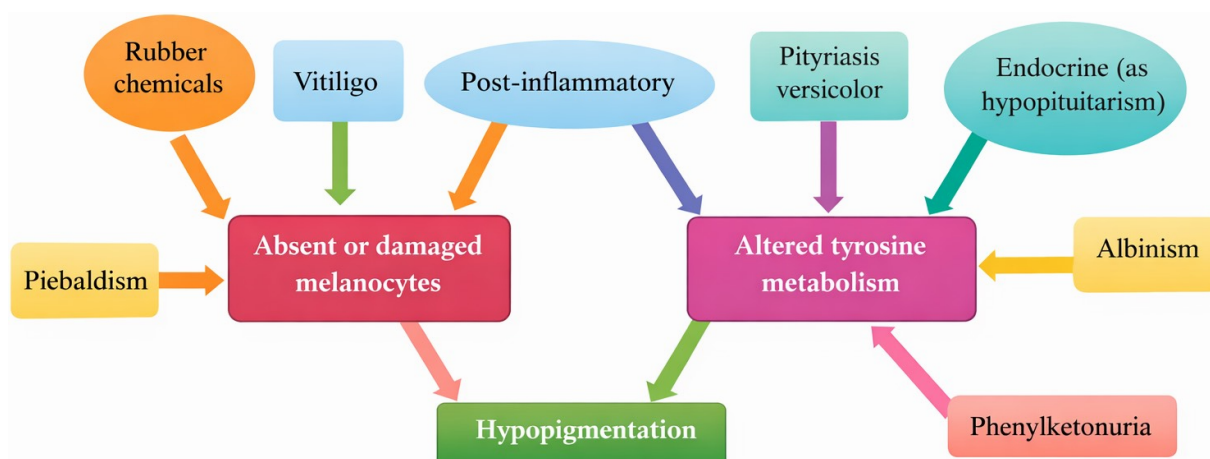


Figure 2. Molecular mechanisms leading to hypopigmentation.

Hypopigmentation can occur either due to loss or damage of melanocytes, as observed in vitiligo and post-inflammatory conditions, or due to impaired melanin synthesis resulting from altered tyrosine metabolism in disorders such as albinism and endocrine abnormalities

VII. Clinical Implications and Future Perspectives

Advances in molecular genetics have significantly improved the clinical understanding and management of pigmentation disorders. In vitiligo, identification of immune-mediated signaling pathways has enabled the development of targeted immunomodulatory therapies. Janus kinase (JAK) inhibitors, which suppress interferon- γ signaling and downstream inflammatory cascades, have demonstrated encouraging repigmentation outcomes and represent a major milestone in vitiligo treatment (Ezzedine et al., 2015).

In albinism, molecular diagnosis through next-generation sequencing has enhanced disease classification, genetic counseling, and early intervention strategies. While curative treatments remain limited, gene-based diagnostics facilitate informed family planning and optimized visual rehabilitation (Montoliu et al., 2014).

For melasma, improved understanding of genetic predisposition, epigenetic regulation, and hormonal signaling has opened new avenues for personalized therapy. Emerging strategies targeting epigenetic modifiers, estrogensignaling, and vascular components hold promise for improving long-term treatment outcomes and reducing recurrence (Passeron and Picardo, 2018).

Future research should focus on elucidating gene-environment interactions, identifying novel

molecular biomarkers, and integrating genomic, epigenomic, and transcriptomic data. Such approaches are expected to refine disease classification, enable personalized therapeutic strategies, and improve patient quality of life.

VIII. Conclusion

Skin pigmentation disorders encompass a diverse group of conditions with complex and multifactorial molecular genetic foundations. Although vitiligo, albinism, and melasma exhibit distinct clinical features, they converge on shared biological pathways governing melanocyte development, survival, and melanin synthesis. Advances in molecular genetics have clarified how genetic susceptibility, signaling dysregulation, and environmental influences interact to shape pigmentation outcomes.

Vitiligo is predominantly driven by immune-mediated melanocyte destruction, albinism results from inherited defects in melanogenic enzymes or melanosomal proteins, and melasma represents a hyperfunctional melanocyte phenotype influenced by hormonal, environmental, and epigenetic factors. These mechanistic differences highlight the necessity of disease-specific diagnostic and therapeutic approaches.

Continued investigation into the molecular genetics of pigmentation disorders will be essential for translating biological insights into effective clinical interventions. Integrative, multi-omics research strategies are likely to accelerate the development of targeted therapies and personalized management, ultimately improving outcomes and quality of life for affected individuals.

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