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REVIEW

Genetics of Vitiligo: A Review

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Abstract: Vitiligo is a common acquired depigmentation skin disease with obvious family aggregation. About 25−50% of patients have positive family history, which belongs to polygenetic disease. In recent years, through candidate genes and genome-wide association studies, multiple susceptibility gene loci have been found, and studies also show that there is genetic heterogeneity among different populations. Environmental factors can also interact with genetic factors to trigger diseases through various mechanisms. The risk assessment model based on genetic and environmental factors provides a new direction for early screening and personalized prevention and treatment. In the future, we need to combine single cell sequencing and other multi omics technologies to explore the mechanism, develop targeted treatment strategies, and strengthen the application of genetic counseling and preventive measures in high-risk populations.

Keywords: vitiligo, genetics, genome, autoimmune

Introduction

Vitiligo is an autoimmune disorder characterized by the selective destruction of melanocytes in the skin and mucous membranes, presenting as localized or generalized white patches. The global prevalence is approximately 0.5–2%, with no significant gender or geographic differences, though slightly higher rates are observed in regions such as India and the Middle East.[1]

Vitiligo is primarily classified into two clinical subtypes, they are non-segmental vitiligo (NSV) and segmental vitiligo (SV). NSV is the most common (accounting for 80–90% of cases), exhibiting symmetrical distribution and often associated with autoimmune diseases (eg, thyroid disorders, type 1 diabetes).[2] SV is relatively rare, follows a dermatomal distribution, has an earlier onset and is less frequently linked to autoimmune conditions.[3,4]

Lesions typically present as well-defined milky-white patches, commonly occurring on the face, hands, limbs, and friction-prone areas (eg, elbows, knees). Disease progression is generally categorized as stable or active, with some patients experiencing worsening due to the Koebner phenomenon.[5]

Although vitiligo is not life-threatening, it profoundly impacts patients' psychological and social well-being. Due to the visibility of lesions, patients often face social stigma, discrimination, and challenges in employment and relationships.[6] Multiple studies indicate that anxiety and depression rates are significantly higher among vitiligo patients, particularly adolescents and females.[7] Additionally, individuals with darker skin tones experience greater psychological burden due to the stark contrast of lesions.[8] Therefore, vitiligo treatment must address both repigmentation and psychological support.

The etiopathogenesis of vitiligo remains multifactorial, with several competing theories proposed. The autoimmune hypothesis posits that melanocytes are targeted by autoreactive T cells, supported by the frequent association with other autoimmune disorders.[9] The oxidative stress theory suggests that excessive reactive oxygen species (ROS) accumulation leads to melanocyte apoptosis.[10] Neurohumoral mechanisms involve neuropeptide-mediated melanocyte damage,[11] while the melanocyte intrinsic defect theory highlights inherent vulnerabilities in melanocyte survival pathways.[12] More recently, viral triggers and genetic predisposition have been integrated into a convergent model, wherein environmental factors interact with

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susceptibility genes to initiate disease.[13] These pathogenic theories provide a framework for understanding the complex genetic and environmental interactions discussed in this review.

Genetic Epidemiology of Vitiligo

Family studies provide direct evidence for the genetic susceptibility of vitiligo. Studies have shown that the risk of vitiligo in first-degree relatives is significantly higher than that in the general population. For example, Alkhateeb et al[1] and other scholars' investigation on 2624 cases of vitiligo probands showed that about 20% of the patients had at least one affected first-degree relative, and the incidence was 10–36 times higher than that of the general population. Zhang et al.[14] Reported a 28.3% familial incidence in the Chinese population, suggesting that there may be stronger familial aggregation in the Asian population. There are differences in disease risk among different kinship. The closer the kinship, the higher the risk of disease. The risk of individual with parents' medical history is about 5–7%; The individual risk of brothers and sisters with medical history is about 6–8%. Nath[15] and other studies further proved that if both parents suffer from vitiligo, the risk of offspring will rise to 30–40%, indicating that the disease has a polygenic cumulative effect.

Twin studies provide key insights into the contribution of genetic factors to vitiligo. Alkhateeb's epidemiological studies[1] showed that the comorbidity rate of monozygotic twins (MZ) was 23−26%, and that of dizygotic twins (DZ) was 4−6%. This significant difference strongly supports the role of genetic factors in the pathogenesis of vitiligo. It is worth noting that even identical twins do not show 100% consistency, indicating that environmental factors (such as stress, skin trauma) may trigger the disease in genetically susceptible individuals.[16] The heritability estimation based on twin data showed that the heritability of vitiligo was about 75−80%, and the remaining 20−25% was attributed to environmental factors. The heritability of autoimmune subtypes may be higher.[17]

There are differences in genetic susceptibility to vitiligo among different races and populations. The global prevalence of vitiligo varies by race. The prevalence rate of Caucasian population is 0.5–1%, that of Asian population is 0.5–2%, that of African population is 1–2.5%, and that of certain groups in some parts of India can be as high as 3–4%. Genome-wide association analysis (GWAS) studies highlighted significant ethnic differences in genetic association. European populations were mainly associated with *HLA-A*02:01, PTPN22* and *TYR* alleles. The contribution of *HLA-A*30:01* and *HLA-DQB1*03 :03* alleles was greater in Asian population.[8] The African population is associated with a unique slev1 locus. Protective alleles (eg, *HLA-A*03:01*) are more common in European populations, which may explain its low incidence.[18,19]

Research Progress

Early Candidate Gene Research

Before the emergence of GWAS technology, there were several different hypotheses about the pathogenesis of vitiligo. The most mainstream theory is the autoimmune theory, with the core idea that melanocytes are mistakenly attacked by the autoimmune system; the oxidative stress theory (accumulation of reactive oxygen species (ROS) in melanocytes leading to apoptosis), neurohumoral theory (neuropeptide mediated melanocyte destruction), and melanocyte intrinsic defect theory (melanocyte intrinsic abnormalities leading to increased vulnerability) are also parallel theories of the same period; the theory of viruses is an emerging hypothesis in recent years, whose core idea is that viral infections trigger cross immune responses. The current academic consensus is the integration theory, which refers to the joint action of multiple factors to cause disease. Based on these hypotheses, the following candidate genes have been selected and studied (Table 1).

GWAS Findings

GWAS has identified numerous susceptibility loci (Table 2). Vitiligo susceptibility loci exhibit both consistency and variability across populations.[13] Among these, the major histocompatibility complex (MHC) region (6p21.32), particularly *HLA-B*33:01*[40] and *HLA-DQB1*,[8,41] shows significant associations in both European and Asian populations, suggesting that HLA-mediated autoimmune responses are a core pathogenic mechanism. Cross-population shared immune-related genes such as *TYK2* (7p15.2), *IL12* (12q13.2) and *IL23* (9p24.1)[42] contribute to disease onset by regulating *Th1*/*Th17* immune responses. Meanwhile, pigment metabolism genes like *TYR* (11q14.3) and

Table 1 Abnormal Expression of Vitiligo Candidate Genes

Chromosomal Location	Gene Symbol	Full Name of Gene	Mutation Site	Susceptible Population	OR Value
1p13.2	*PTPN22*[20,21]	Protein tyrosine phosphatase, non-receptor type 22	rs2476601	Europe (Northern Europe > Southern Europe; no association in East Asia)	2.16
2q33.2	*CTLA4*[22]	Cytotoxic T lymphocyte-associated protein 4	rs231775(A/G)	The CTLA4 gene variant is associated with susceptibility to vitiligo only in the European population.	1.45
3p13	*FOXP1*[13,23]	Fork head frame P1	rs17008723(A/C)	Global population	1.33
4q27	*IL2*[24,25]	Interleukin 2	rs2069763(A/C)	Global population	0.37
5q31.1	*IL4*[26]	Interleukin 4	rs2243250(−590C/T)	Global population	-
6p21.3	*HLA*[27]	Human leukocyte antigen	HLA-A*02 Increase in frequency; HL A-A*11/DRB1*01 Frequency Reduction	Global population	1.60; 0.46/ 0.39
6q15	*BACH2*[9,28]	BTB domain and CNC homolog 2	rs3757247(G/A)	Global population	1.20
9q23	*TYRP1*[29]	Tyrosinase related protein 1	rs2733832	Being studied as a potential site	-
10p15.1	*IL2RA*[18,24]	Interleukin-2 receptor alpha chain	rs706779(A/G)	Global population	1.27
10q25.3	*CASP7*[9]	Caspase 7	rs3814231(G/A)	Global population	0.81
10q26.3	*miR-202*[30]	MicroRNA-202	rs12355840(C/T)	Global Population	1.64
11q21	*TYR*[31]	Tyrosinase	rs4409785(T/C)	European descent	1.34
12q13.2	*IKZF4*[9]	IKAROS family zinc finger protein4	rs1701704(A/C)	Global population	1.29
14q32.33	*GZMB*[32]	Granzyme B	rs8192917	Global Population	1.28
15q12-q13.1	*OCA2-HERC2*[9,33]	Ocular skin albinism type II	rs1129038(T/C)	East Asia (Southern China>Northern China)	1.22
15q13-q14	*miR-211*[30]	MicroRNA-211	rs8039189(G/T)	Global Population	0.47

(*Continued*)

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Table 1 (Continued).

Chromosomal Location	Gene Symbol	Full Name of Gene	Mutation Site	Susceptible Population	OR Value
16q24.3	*MC1R*[9,34]	Melanocortin-1 receptor	rs4785587(G/A)	Europe (Ireland, Scotland red haired population)	0.80
17p13.2	*NLRP1*[31]	The NLR family's Pyrin domain contains 1	rs2670660(T/C)	Populations of the United States, the United Kingdom, Romania, Jordan, and India	2.96
17q21.2	*STAT3*[35,36]	Signal transducer and activator of transcription 3	rs744166(T/C)	European descent	1.90
19p13.3	*TICAM1*[9,37]	Toll like receptor adaptor molecule 1	rs6510827(C/T)	Global Population	1.19
20q11.22	*ASIP*[38]	Agouti signaling protein	rs6059655(G/A)	European descent	0.61
Xq13.1	*CXCR9/10*[39]	C-X-C chemokine receptor 3	(The changes are still disputed, but they are generally considered to be associated with vitiligo)	Global Population	-

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Table 2 GWAS Discovers Susceptible Gene Micro Stores

Chromosome	SNP ID	-log10 (p)	Candidate Genes/Regions	Susceptible Person
1p13.2	rs2476601	7.0	*PTPN22*[43]	European descent (No association in the Asian population)
1p36.32	rs301819	8.3	*RERE*[18,44]	Han Chinese
2q33.2	rs3184504	17.1	*SH2B3*[9,45]	Han Chinese
4q24	rs12203592	17.0	*IRF4*[35]	Multi population (Europe, Asia)
6p21.32	rs11966200	11.3	*HLA-B(MHC region)*[9,40]	Asia, Europe
6q15	rs3757247	7.5	*BACH2*[28]	European descent
9p24.1	rs11209026	3.5	*IL23R*[42]	Multi population
10q22.3	rs1250544	7.8	*ZMIZ1*	Han Chinese
11q14.3	rs4409785	12.8	*TYR*[29]	European descent
12q13.2	rs2288831	9.6	*IL12B*[46]	European descent
14q12	rs8192917	7.5	*GZMB*[18,47]	Han Chinese
16q24.3	rs4785587	13.0	*MC1R*[9,34]	Europe descent (Individuals with red hair background)
21q22.3	rs11203203	8.8	*UBASH3A*[23]	European descent

*MC1*R (16q24.3) are associated with vitiligo risk across all populations, though *TYR* shows a stronger association in Asians.[29]

Population-specific loci include *ZMIZ1* (10q22.3)[48] and *GZMB* (14q12),[49] which are particularly significant in the Chinese Han population, likely due to their roles in regulating T-cell differentiation and cytotoxicity. In contrast, *FOXD3* (1p13.2)[42] and *PTPN22* (1p13.2)[19] are more prominent in European populations, reflecting differences in neural crest development and B-cell regulation.

Functionally, these loci are involved in the pathogenesis through three major pathways. First, *HLA* mediated antigen presentation activates $CD4^{+}T$ cells, and cytokines such as *IL23R*/*IL12B*[50] can drive *Th17* inflammatory response; Secondly, the mutation of pigment related genes (such as *TYR* and *MC1R*) will lead to melanocyte stress and antigen release. In addition, *GZMB*, which is unique to Asian people, can directly induce melanocyte apoptosis through granzyme B; Finally, the genetic variation of *BACH2* (6q15) may destroy immune tolerance. These findings not only reveal the complex genetic background of vitiligo but also provide an important basis for the development of precision medical strategies for different populations.

Genetic Mechanisms

Gene–Environment Interactions

Environmental factors significantly influence vitiligo onset through gene–environment interactions (G×E), which regulate the expression of susceptibility genes. Ultraviolet (UV) exposure is a classic environmental trigger that activates immune responses via oxidative stress and DNA damage pathways, thereby modulating vitiligo-related genes (eg, *TYR, PTPN22*, and *NLRP1*) and contributing to disease manifestation. For instance, UV radiation induces keratinocytes to release pro-inflammatory factors, leading to the exposure of melanocyte-specific antigens and triggering autoimmune attacks.[42] Additionally, GWAS studies have revealed that *MC1R* gene variants (associated with skin pigmentation) synergistically increase vitiligo risk when combined with UV exposure, suggesting a genotype-environment correlation.[13]

Chemical agents (eg, phenolic compounds, hydroquinone) interfere with melanocyte function through epigenetic modifications or direct toxicity, altering the expression of susceptibility genes. Research indicates that occupational exposure to such chemicals is closely linked to polymorphisms in catalase (*CAT*) and vitamin D receptor (*VDR*) genes, which activate oxidative stress pathways and promote melanocyte apoptosis. For example, hydroquinone suppresses the expression of microphthalmia-associated transcription factor (*MITF*), disrupting melanocyte survival and differentiation —a mechanism particularly pronounced in individuals carrying the *PTPN22* risk allele.[19]

Psychological stress modulates the immune microenvironment via neuroendocrine pathways (eg, Hypothalamic-Pituitary-Adrenal (*HPA)* axis activation), influencing vitiligo susceptibility genes. Chronic stress elevates cortisol levels, stimulating the release of pro-inflammatory cytokines (eg, *IL-6, TNF-α*) and exacerbating autoimmune responses. Studies show that individuals with specific variants of the catechol-O-methyltransferase (*COMT*) gene are more prone to melanocyte-specific T-cell activation under prolonged stress, likely due to epigenetic regulation (eg, DNA methylation).[11]

Gene Networks and Pathway Abnormalities

Vitiligo is a complex polygenic disorder involving interactions among susceptibility genes across multiple pathways, including cell signaling, immune regulation, and melanocyte development, ultimately leading to melanocyte destruction or dysfunction. Below is a molecular-level summary of key genes and their networks.

In terms of gene interactions in cell signaling pathways, vitiligo susceptibility genes (such as *PTPN22, STAT4* and *IFIH1*) jointly regulate signal transduction in immune cells and melanocytes. Specifically, the lymphoid specific protein *TYR*osine phosphatase (*LYP*) encoded by *PTPN22* gene, whose function acquired mutations (such as *R620W*) can enhance the signal transduction of T cell receptor (*TCR*), thus promoting the activation of self-reactive T cells.[51] At the same time, *STAT4* gene mediates the signal transmission of interferon-γ (*IFN-γ*) through *JAK-STAT* pathway, up regulates the production of C-X-C Motif Chemokine Ligand 10 (*CXCL10)* and other chemokines, and then recruits cytotoxic $CD8^+$T cells to attack melanocytes.[9] In addition, *IFIH1* gene (also known as *MDA5*) is responsible for detecting viral RNA in cells, stimulating the production of type I interferon by activating Mitochondrial Antiviral Signaling Protein (*MAVS*)-Interferon Regulatory Factor (*IRF*)3/7 pathway, and finally amplifying the immune response.[52] The abnormal activation of these genes laid the foundation for the immunological pathogenesis of vitiligo.

In the link between immune regulatory genes and the collapse of autoimmune tolerance, the core mechanism of vitiligo is the destruction of melanocytes mediated by autoimmune response, which is mainly driven by key genes such as nlrp1, *FOXP3* and *CTLA4*. First, nlrp1 gene encodes a key component of inflammasome, and its mutation will lead to the excessive release of interleukin-1 β (*IL-1 β*) and *IL-18*, thus creating a pro-inflammatory microenvironment.[16] More importantly, *FOXP3*, as the main transcription factor of regulatory T cells (*Treg*), its reduced expression or dysfunction will weaken the immunosuppressive function, resulting in the escape of self-reactive cells such as MELAN-A-specific $CD8^+$T cells from the tolerance mechanism.[53] It is also important that *CTLA4* gene maintains peripheral immune tolerance by inhibiting the costimulatory signal of T cells, and its single nucleotide polymorphisms (*SNPs*) are closely related to the risk of vitiligo.[54]

As for the role of melanocyte self-development and oxidative stress defense genes, their survival and function depend on key genes such as *MITF. MITF* is the core regulator of melanocyte development, and its downstream target *Tyr*osinase (*TYR*) dominates the biosynthesis of melanin. Therefore, the mutation or low expression of *TYR* will directly lead to pigmentation dysfunction. Especially, oxidative stress plays a central role in this process.[12] The deficiency of catalase (*CAT*) and superoxide dismutase 2 (*SOD2*) can significantly increase the sensitivity of melanocytes to hydrogen peroxide (H_2O_2) and then cause endoplasmic reticulum stress and apoptosis.[10] In addition, the genetic variation of vitamin D receptor (*VDR*) may also interfere with the calcium signal transduction in melanocytes and weaken their antioxidant capacity.[55]

Finally, these genes are not acting in isolation, but constitute a dynamic gene pathway regulatory network and provide targets for treatment. For example, MITF can up regulate the anti apoptotic protein *BCL2* to maintain the survival of melanocytes, and oxidative stress can inhibit the activity of *MITF* by activating NF-κB pathway, which forms a vicious circle.[56] On the other hand, the abnormal expression of immune checkpoint molecules (such as *PD-1*/*PD-L1*) will further aggravate T cell-mediated cytotoxicity.[57] These in-depth mechanism studies provide directions for the development of

targeted therapies, such as the use of *JAK* inhibitors to block IFN-γ signaling pathway, the use of antioxidants such as N-acetylcysteine, and *Treg* amplification therapy.[58]

Epigenetic Factors

The development and progression of vitiligo are not only associated with genetic predisposition but are also significantly influenced by epigenetic modifications (eg, DNA methylation, histone modifications). These modifications regulate gene expression and participate in key pathological processes such as melanocyte dysfunction, autoimmune responses, and oxidative stress.

DNA methylation is one of the most in-depth research fields in the epigenetic mechanism of vitiligo. Studies have shown that melanocytes and surrounding keratinocytes in patients with vitiligo have global hypomethylation, which leads to the up regulation of IFN-γ, *CXCL10* and other pro-inflammatory genes, and then recruit self-reactive T cells to attack melanocytes.[59] At the same time, hypermethylation in the promoter region of *FOXP3* gene (the core gene regulating the function of *Treg* cells) will inhibit its expression, thus weakening the immune tolerance and promoting the autoimmune response.[60] In addition, aberrant methylation of key genes such as *MITF* and *TYR* in melanocytes may interfere with melanin synthesis and further aggravate depigmentation.[61] These findings jointly reveal the key role of DNA methylation imbalance in vitiligo immune imbalance and melanocyte dysfunction.

In the regulation of histone modification on vitiligo related genes, acetylation, methylation and other modifications regulate the transcriptional activity of susceptible genes by changing the chromatin structure. Specifically, overexpression of histone deacetylases (*HDACs*) can inhibit *MITF* and anti apoptotic gene *BCL2*, thereby promoting melanocyte apoptosis.[34] More importantly, in $CD8^+$T cells, the enrichment of inhibitory histone marker *H3K27me3* on immune checkpoint genes such as *PD-1* may enhance its aggressiveness to melanocytes.[62] On the other hand, the decreased activity of histone acetyltransferases (*HATS*) may lead to the down-regulation of the expression of *Nrf2*, a key antioxidant factor, and increase the sensitivity of melanocytes to oxidative stress.[63] These modifications together shape the epigenetic landscape of vitiligo and continue to affect the progress of the disease.

In view of the reversibility of epigenetic modification, drugs targeting DNA methylation or histone modification (such as *HDAC* inhibitors and demethylation drugs) are expected to provide new therapeutic strategies. For example, DNA demethylation drug 5-azacytidine can restore the expression of *FOXP3*, thereby enhancing the function of regulatory T cells.[64] *HDAC* inhibitors (such as vorinostat) may promote the survival of melanocytes by up regulating the expression of *MITF*. These studies laid a theoretical foundation for the development of epigenetic targeted therapy.[65]

The current research has formed a more objective system (Figure 1). It still needs to be pointed out that future research should further explore the interaction between environmental factors and epigenomes, which will not only help to deepen the understanding of the pathogenesis of vitiligo, but also provide a new direction for the development of personalized intervention strategies.

Establishment and Application of Genetic Risk Assessment Models for Vitiligo

Vitiligo risk assessment models integrate GWAS-identified susceptibility genes (eg, *NLRP1, PTPN22, TYR*) and environmental exposure data (UV radiation, chemical contact, psychological stress, etc).[66] These models use multivariate regression or machine learning algorithms to calculate individual disease risk. Clinical applications include screening high-risk populations (eg, those with a family history) and formulating personalized prevention strategies (eg, enhanced photoprotection or antioxidant therapy).[8] Early intervention based on these models may reduce disease risk by 30–50%.[67]

However, the current model shows obvious limitations. Genetic factors accounted for only 25% of the disease risk.[68] Due to the need for real-time tracking, environmental assessment faces challenges in data integration.[69] The molecular mechanism of gene environment interaction has not been fully elucidated.

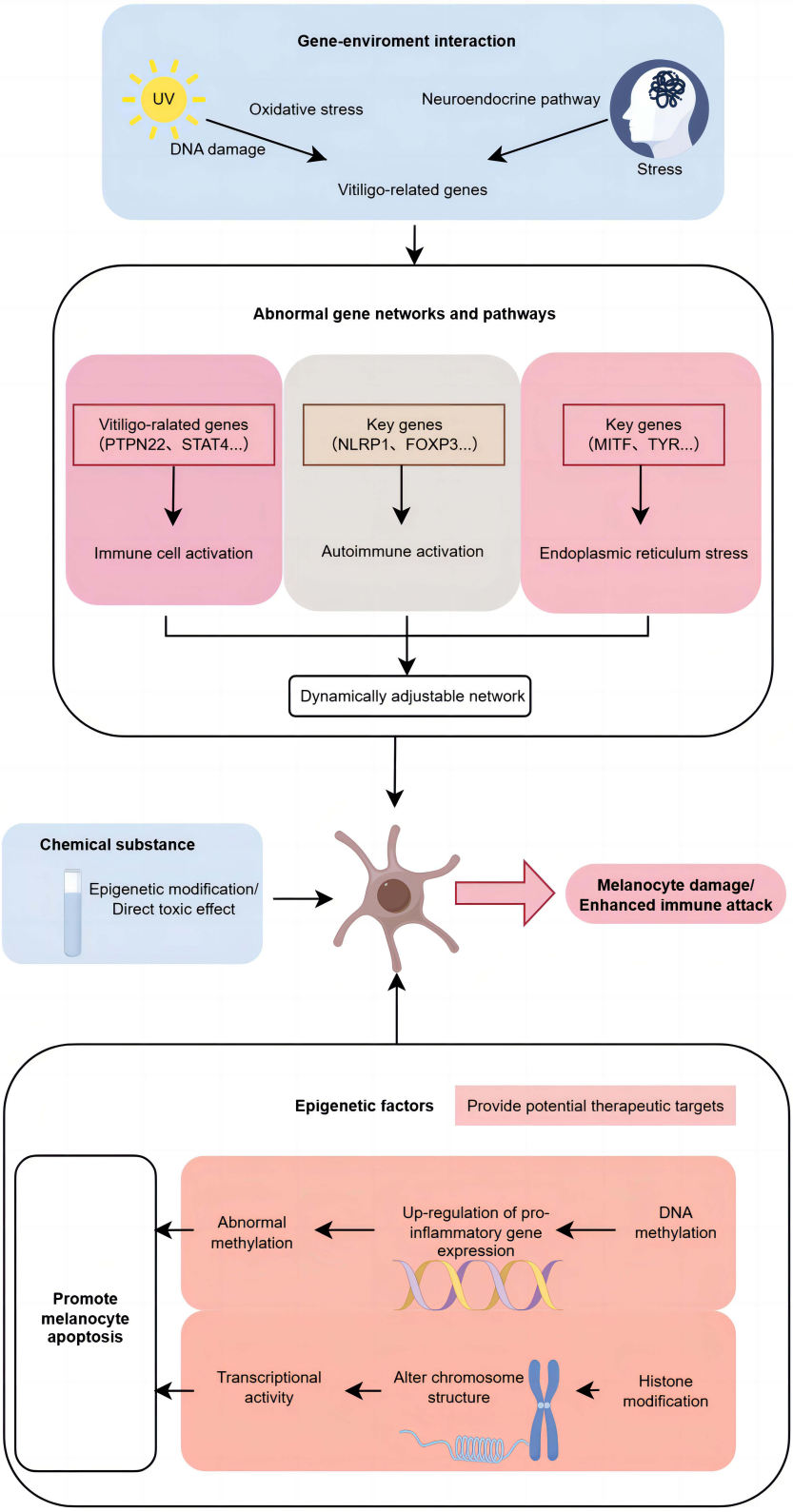

Figure 1 A proposed mechanistic framework for vitiligo pathogenesis integrating genetic susceptibility, environmental triggers, and epigenetic dysregulation.

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Future Research Directions and Perspectives

Application of Novel Technologies in Vitiligo Genetic Research

Emerging technologies are reshaping vitiligo research. Single-cell RNA sequencing (scRNA-seq) has uncovered aberrant interactions between $CD8^+$ T cells and melanocytes in lesions, identifying novel immune-related gene clusters (eg, *CXCL10*$^+$, $CD8^+$, T-cell, subsets).[65] Multi-omics integration (epigenomics, proteomics) with GWAS revealed that noncoding variants (eg, rs11966200) may regulate *MITF* expression, affecting melanocyte function.[13] Besides, *CRISPR-Cas9* generated *NLRP1*-mutant mouse models, confirming its role in inflammasome-mediated autoimmunity.[70] These approaches promise to uncover new therapeutic targets and advance precision medicine.

Implications of Genetic Research for Vitiligo Treatment

Targeted therapies based on genetic insights are gaining traction. *JAK* inhibitors (eg, tofacitinib), which block the *JAK-STAT* pathway (linked to *STAT4*/*IFNGR2*), significantly improve repigmentation.[71] Besides, *MITF* agonists (eg, *α-MSH* analogs) aim to restore melanocyte function in patients with low *MITF* expression.[72]

In terms of individual treatment, *HLA-DRB1*04* carriers respond better to immunotherapy (eg, *PD-1* inhibitors), while *TYR* mutation patients may benefit from antioxidant combos.[73]

Genetic Insights for Vitiligo Prevention

Polygenic risk scores (eg, based on *PTPN22*/*IL2RA SNPs*) identify high-risk individuals (70% accuracy for family history-positive cases).[8]

Epigenetic clock analysis suggests UV protection may delay DNA methylation aging in high-risk children, reducing disease risk.[61] Prospective cohort studies are needed to validate prevention strategies.

The Evolving Role of Genetic Counseling

Genetic counseling for vitiligo is shifting from empirical judgment to a precise model based on molecular genetics. First, through the gene screening of high-risk groups (such as those with family history) and the evaluation combined with polygene risk model.[74] Secondly, genotypes are used to predict disease progression and drug response, for example, *JAK-STAT* pathway variation is used to predict the sensitivity to *JAK* inhibitors.[75] Finally, provide personalized lifestyle suggestions and early intervention strategies. With the improvement of the accessibility of gene testing, genetic counseling based on genome-wide association analysis (GWAS) will gradually become the core component of clinical management[74] and promote the transformation of diagnosis and treatment strategies from passive treatment to active prevention.

Conclusion

This review synthesizes current knowledge on the genetic architecture of vitiligo, underscoring its high heritability (~80%) and polygenic nature. Family and twin studies robustly support a strong genetic component, while GWAS has identified numerous susceptibility loci within immune regulation (eg, *HLA*, *PTPN22*), pigmentation (eg, *TYR*, *MC1R*), and apoptosis pathways, with notable ethnic heterogeneity. Gene–environment interactions, particularly involving UV exposure, chemical agents, and psychological stress, modulate disease expression through epigenetic and transcriptional mechanisms.

Emerging technologies—such as single-cell sequencing, multi-omics integration, and CRISPR-based models—are deepening our understanding of vitiligo pathogenesis and revealing novel therapeutic targets. The development of polygenic risk scores and epigenetic-based interventions holds promise for personalized prevention and treatment strategies. Moving forward, integrating genetic counseling with molecular profiling will facilitate early identification of high-risk individuals and enable precision medicine approaches, ultimately improving clinical outcomes and quality of life for patients with vitiligo.

What is Already Known?

Vitiligo is a polygenic autoimmune disease with high heritability (~80%). GWAS has identified numerous susceptibility loci in *HLA*, immune regulation (eg, *PTPN22*), and pigmentation (eg, *TYR*) pathways, showing significant ethnic heterogeneity. Environmental triggers like UV exposure interact with genetic factors.

What Does This Study Add?

This review synthesizes recent advances, highlighting population-specific genetic risks, gene–environment interaction mechanisms, and epigenetic dysregulation. It outlines future directions, including polygenic risk scores, novel therapeutics (eg, *JAK* inhibitors), and the application of single-cell technologies for precision.

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