GENETIC BASIS AND CLINICAL MANIFESTATIONS OF ALBINISM

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Abstract. *Albinism is a heterogeneous group of inherited disorders characterized by a significant reduction or complete absence of melanin pigmentation in the skin, hair, and eyes. The condition arises from genetic defects affecting melanin biosynthesis, melanosomal structure, or intracellular transport processes within melanocytes. In addition to pigmentation abnormalities, albinism is associated with characteristic developmental defects of the visual system, leading to lifelong visual impairment.*

This article presents a comprehensive review of the molecular genetic mechanisms underlying albinism, its pathogenesis, major clinical subtypes, and ophthalmological manifestations. Mutations in the TYR, OCA2, TYRP1, SLC45A2, and GPR143 genes are identified as the principal genetic determinants of both oculocutaneous and ocular forms of albinism. Clinically, reduced visual acuity, photophobia, nystagmus, foveal hypoplasia, and abnormal optic nerve fiber decussation represent the most significant functional impairments.

The review highlights the importance of early diagnosis, molecular genetic testing, genetic counseling, and multidisciplinary clinical management in improving visual outcomes and quality of life for individuals with albinism.

Key words: *albinism, melanin, molecular genetics, tyrosinase, clinical manifestations, ophthalmology.*

Introduction

Albinism is among the most extensively studied hereditary pigmentation disorders, yet it remains clinically and genetically complex. The disorder is caused by impaired melanin synthesis despite the presence of a normal number of melanocytes in the skin, hair follicles, and eyes [1,11]. Melanin is a critical biological pigment responsible not only for coloration but also for protection against ultraviolet (UV) radiation and for the normal development of ocular structures during embryogenesis.

The absence or reduction of melanin during critical stages of development disrupts retinal maturation and optic nerve pathway formation. As a result, individuals with albinism commonly experience visual disturbances that persist throughout life. Epidemiological studies indicate that albinism occurs worldwide with an estimated prevalence of approximately 1 in 17,000 individuals; however, in certain African populations, the prevalence may reach 1 in 1,000 due to genetic and sociocultural factors [2,16].

Beyond its medical consequences, albinism poses substantial psychological, social, and economic challenges. Individuals with albinism often face stigmatization, discrimination,

and limited access to healthcare, particularly in low-resource settings. Therefore, albinism represents not only a medical condition but also a significant public health and social issue.

The aim of this article is to provide an in-depth analysis of the genetic basis, pathophysiological mechanisms, and clinical manifestations of albinism based on contemporary scientific literature.

Materials and Methods

This study is based on a comprehensive retrospective review of scientific literature, including authoritative textbooks, meta-analyses, and peer-reviewed articles published in the fields of molecular genetics, dermatology, and ophthalmology [3,48]. Publications were selected using standardized inclusion criteria focusing on genetic mechanisms, clinical presentation, and diagnostic strategies related to albinism.

Data were systematically categorized according to molecular genetic pathways, clinical subtypes, dermatological and ophthalmological manifestations, and genotype–phenotype correlations. Additionally, results from clinical and observational studies involving patients with various forms of albinism were analyzed to assess phenotypic variability associated with specific gene mutations [4,92].

Results

Molecular Genetic Basis of Albinism

Albinism is predominantly inherited in an autosomal recessive manner, although X-linked inheritance has been documented, particularly in ocular albinism [5,27]. The disorder results from mutations in genes encoding enzymes, transporters, and structural proteins essential for melanin biosynthesis and melanosome function.

The TYR gene encodes tyrosinase, the key enzyme responsible for catalyzing the initial and rate-limiting steps of melanin synthesis, including the conversion of tyrosine to DOPA and DOPAquinone. Mutations in TYR lead to a marked reduction or complete absence of enzymatic activity, resulting in severe hypopigmentation [6,89].

The OCA2 gene plays a critical role in regulating melanosomal pH and maintaining optimal conditions for tyrosinase activity. Defects in this gene result in decreased melanin production and variable pigmentation phenotypes [7,43]. The TYRP1 gene contributes to eumelanin synthesis and stabilization of tyrosinase, influencing pigment quality and color [8,68].

The SLC45A2 gene encodes a transmembrane transporter involved in ion homeostasis within melanosomes. Mutations in this gene disrupt melanosomal function and are associated with lighter pigmentation and pronounced ocular involvement. X-linked ocular albinism is primarily caused by mutations in the GPR143 gene, which affects melanosome biogenesis in retinal pigment epithelium cells.

Clinical Manifestations and Pathophysiology

The clinical manifestations of albinism can be broadly divided into dermatological and ophthalmological features. Dermatological signs include diffuse hypopigmentation of the skin and hair, increased susceptibility to sunburn, and a significantly elevated risk of actinic

damage and skin malignancies, particularly squamous cell carcinoma and basal cell carcinoma [1,22].

Ophthalmological manifestations constitute the most disabling aspect of albinism. Melanin deficiency during ocular development leads to abnormal retinal differentiation, resulting in foveal hypoplasia and reduced cone density. Consequently, patients experience decreased visual acuity, often ranging from moderate to severe impairment [10,74].

Additional ocular features include nystagmus, strabismus, photophobia, and impaired stereoscopic vision. Abnormal decussation of optic nerve fibers at the optic chiasm further contributes to visual dysfunction and altered binocular processing [9,61]. The severity of these manifestations varies depending on the underlying genetic mutation and residual melanin production.

Discussion

The findings of this review demonstrate that although albinism is primarily a monogenic disorder, it exhibits considerable clinical heterogeneity. This variability reflects complex genotype–phenotype relationships, modifier genes, and environmental influences affecting melanin production and ocular development [4,115].

Recent advances in molecular diagnostic techniques, including next-generation sequencing, have significantly improved the detection of causative mutations. Accurate genetic diagnosis enables better prognostic assessment, personalized management strategies, and informed genetic counseling for affected families [11,83].

Early diagnosis is essential for initiating preventive measures such as photoprotection, regular dermatological surveillance, and early visual rehabilitation. Low-vision aids, refractive correction, and educational support play a crucial role in maximizing functional outcomes and social integration.

Conclusion

Albinism is a complex hereditary disorder resulting from genetic defects in melanin biosynthesis and melanosomal function. Mutations in the TYR, OCA2, TYRP1, SLC45A2, and GPR143 genes are central to disease pathogenesis. Clinically, albinism is characterized by pigmentation abnormalities and significant visual system defects that profoundly affect quality of life.

Early diagnosis, molecular genetic testing, multidisciplinary clinical management, and appropriate social support are essential for optimizing long-term outcomes for individuals with albinism.

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