ALBINISM

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**ABSTRACT**

Albinism is a rare [genetic](https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/genetics) disorder affecting about 1 in 17,000 people worldwide. Three main types of albinism can be clinically eminent oculocutaneous, ocular, and syndromic (Hermansky-Pudlak syndrome and Chediak-Higashi syndrome).The main defect of albinism is caused by melanin deficiency. A distinct disorder, FHONDA (Foveal Hypoplasia, Optic Nerve Decussation defects and Anterior segment dysgenesis) shares phenotypic characteristics with these conditions. The degree of skin [hypopigmentation](https://www.sciencedirect.com/topics/medicine-and-dentistry/hypopigmentation) in albinism is virtually variable and some [patients](https://www.sciencedirect.com/topics/medicine-and-dentistry/patient) are normally pigmented. Ocular signs are at the vanguard and include foveal [hypoplasia](https://www.sciencedirect.com/topics/medicine-and-dentistry/hypoplasia), fundal hypopigmentation, iris [transillumination](https://www.sciencedirect.com/topics/medicine-and-dentistry/transillumination), nystagmus, reduced [visual acuity](https://www.sciencedirect.com/topics/medicine-and-dentistry/visual-acuity), reduced or absent [stereopsis](https://www.sciencedirect.com/topics/medicine-and-dentistry/stereoscopic-vision), strabismus, and [refractive errors](https://www.sciencedirect.com/topics/medicine-and-dentistry/refractive-error). At least 20 genes are involved in the different forms of this condition and genetic testing is increasingly being used as a frontline diagnostic tool for this group of disorders.

**I. INTRODUCTION**

Albinism was first discovered in 1908 by a British physician named Sir Archibald Edward Garrod. Albinism is a rare genetic condition caused by mutations of certain genes that affect the amount of melanin your body produces. Melanin controls the pigmentation (color) of your skin, eyes and hair. People with albinism have extremely pale skin, eyes and hair. They are at an increased risk of vision, skin and social issues. Albinism refers to a heterogeneous group of hypopigmentation disorders that share an absolute or relative inherited deficiency of the pigment melanin that leads to characteristic changes in the skin, hair, and visual system (eyes and optic tracts). Melanin is produced and contained within melanosomes, intracellular organelles that are present in the stratum basale of the epidermis, hair bulbs, and intraocular epithelia. Most individuals with albinism have a simple, or nonsyndromic, form that affects the visual system, hair, and skin (oculocutaneous albinism, OCA) or mainly the visual system (ocular albinism, OA). Less commonly, individuals may have a complex, or syndromic, form of albinism that includes a distinctive pattern of organ involvement in addition to OCA. In recent years, much progress has been made in understanding the clinical features, pathophysiology, and molecular basis of albinism.

**II. DIFFERENT TYPES OF ALBINISM**

* brown oculocutaneous albinism
* minimal pigment oculocutaneous albinism
* OCA1
* OCA1A
* OCA1B
* OCA3
* OCA4
* oculocutaneous albinism type 1B
* platinum oculocutaneous albinism
* rufous oculocutaneous albinism
* temperature-sensitive oculocutaneous albinism
* tyrosinase-negative oculocutaneous albinism
* tyrosinase-positive oculocutaneous albinism
* tyrosinase-related OCA
* yellow oculocutaneous albinism
* OCA5
* OCA6
* OCA7
* oculocutaneous albinism type 1A

**Oculocutaneous albinism**:

Oculocutaneous (pronounced “ock-you-low-kew-TAIN-ee-us”) albinism, or OCA, is the most common type of albinism. People with OCA have extremely pale hair, skin and eyes. There are seven different subtypes of OCA, caused by mutations in one of seven genes (OCA1 to OCA7).

* **Ocular albinism**: Ocular albinism, or OA, is much less common than OCA. Ocular albinism affects only your eyes. People with OA usually have blue eyes. Sometimes your irises (colored part of your eyes) are very pale, so your eyes may appear red or pink. This is because the blood vessels inside your eyes show through the irises. Your skin and hair color are usually normal.
* **Hermansky-Pudlak syndrome**: Hermansky-Pudlak syndrome, or HPS, is a type of albinism that includes a form of OCA along with [blood disorders](https://my.clevelandclinic.org/health/diseases/21545-blood-disorders), [bruising](https://my.clevelandclinic.org/health/diseases/15235-bruises) issues and lung, kidney or bowel diseases.
* **Chediak-Higashi syndrome**: Chediak-Higashi syndrome is a type of albinism that includes a form of OCA along with immune and neurological issues.

**a) Oculocutaneous Albinism Type I (OCA1)**

Oculocutaneous albinism type 1 (OCA1) is associated with reduced production of melanin in the skin, hair and eyes. There are two types of OCA1. Individuals affected with OCA1A have a complete absence of melanin pigment resulting in white hair and white skin at birth and irises that do not become darker over time. Visual acuity in individuals can range from 20/200 to 20/400. Individuals with OCA1B have white or light yellow hair at birth that can darken over time, white skin that darkens over time and irises that may change from light blue to green or brown over time. Vision is usually better in individuals with OCA1B than in those with OCA1A.

OCA1 is associated with abnormalities (mutations) in the tyrosinase (TYR) gene. The TYR gene is responsible for the production of the enzyme tyrosinase which is the key enzyme in the formation of melanin pigment. Some TYR mutations result in the production of a completely nonfunctioning tyrosinase enzyme and no melanin pigment is formed. This results in OCA1A. Different TYR mutations result in the production of a tyrosinase enzyme with limited enzymatic activity but it is still able to produce small amounts of melanin pigment. This type of OCA1 is called OCA1B. In the case of OCA1B, melanin pigment will accumulate with time in the skin, hair and eyes.

**b) Oculocutaneous Albinism Type II (OCA2)**

Oculocutaneous albinism type II (OCA2) is associated with the same vision problems that occur in OCA1. Individuals with OCA2 have a wide range of skin pigmentation that is partially dependent on their genetic background of the affected individual and the mutations present. Hair color is usually not completely white and there can be some pigment present in the skin but skin color is usually lighter than in unaffected relatives. Individuals with extensive sun exposure can develop pigmented nevi and lentigines (dark spots on the skin). This does not occur with other types of OCA. A reduction in skin pigment is apparent in Africans and African-Americans but skin coloration appears close to normal in other populations with normally lighter skin pigmentation but affected individuals do not tan. Brown OCA is a type of OCA2 where hair and skin coloration is darker. This type of OCA2 has only been reported in individuals with African ancestry.

OCA2 is associated with mutations in the OCA2 gene (also called the P gene). The OCA2 gene is responsible for production of the OCA2 protein. The precise function of the OCA2 protein is unknown, but it is thought to be important in regulating the movement of the substrate tyrosine into the melanosome as well as regulating the internal environment of the melanosome.

**c) Oculocutaneous Albinism Type III (OCA3)**

Oculocutaneous albinism type III (OCA3) was initially described in the African population. Affected individuals have red to reddish-brown skin, ginger or reddish hair, and hazel or brown eyes and the condition was initially termed rufous albinism. OCA3 has now been identified in several additional populations including those of Asian descent (Chinese and Japanese), Asian Indian and Northern European. Affected individuals of Asian heritage can have blond hair with light brown eyebrows with skin lighter than their parents. Both hair and skin pigmentation increases with age. Reduction in visual acuity is not as severe as in OCA1 or OCA2. Nystagmus and photophobia may not be present.

OCA3 is associated with mutations in the tyrosinase related protein 1 (TYRP1) gene. This gene is responsible for the production of tyrosinase-related protein-1, an enzyme like tyrosinase, which is involved in the production of melanin. The TYRP1 enzyme is part of a gene family that includes tyrosinase and the tyrosinase related protein-2 (TYRP2), all of which are enzymes involved in melanin biosynthesis. The TYRP1 enzyme is responsible for later steps (after the initial tyrosinase step) in melanin pigment production.

**d) Oculocutaneous Albinism Type IV (OCA4)**

Oculocutaneous albinism type IV (OCA4) is characterized by physical features that are similar to those of OCA2. Hair color of affected individuals can range from yellow to brown. Visual acuity can range from 20/30 to 20/400 depending on the amount of pigment that is present, but acuity is usually in the range of 20/100 to 20/200. OCA4 was initially identified in an individual of Turkish origin and has been also found in Asian populations including Japanese and Korean and German individuals.

OCA4 is associated with mutations in the SLC45A2 gene (also called the membrane-associated transporter protein; MATP). The SLC45A2 gene is responsible for the production of a membrane associated transporter protein formed with 12 transmembrane helices. The precise function of this protein is unknown but it is required for the normal production of melanin by the melanocyte.

**e) Oculocutaneous Albinism Type V (OCA5)**

Oculocutaneous albinism type V (OCA5) has been found in only one family in Pakistan. Affected individuals have golden colored hair, white skin and the same visual problems that occur in OCA1. Visual acuity in this family was 6/60.

The gene responsible for OCA5 has been located on chromosome 4 (4q24). 14 genes are in this location, but the specific causative gene for OCA5 has not yet been determined.

**f) Oculocutaneous Albinism Type VI (OCA6)**

Oculocutaneous albinism type VI (OCA6) is characterized as having golden to light to dark brown hair, white skin and brownish irides and has been classified as autosomal recessive ocular albinism (AROA), though individuals are hypopigmented when compared to their parents. Only a few individuals have been identified with this type of albinism and all of the clinical features of OCA6 have not been determined but it is assumed that the reduction in visual acuity will not be as severe as seen in OCA1.

OCA6 is associated with mutations in the SLC24A5 gene. The SLC24A5 gene is responsible for the production of a membrane associated transporter protein. The precise function of this protein is unknown but it belongs to a family of potassium-dependent sodium/calcium exchangers. It may be involved in the maturation of melanosomes.

**g) Oculocutaneous Albinism Type VII (OCA7)**

Oculocutaneous albinism type 7 (OCA7) is characterized with blond to dark brown hair and skin which is more hypopigmented than parents. Individuals had nystagmus and iris transillumination. Visual acuity ranges from 6/18 to 3/60.

OCA7 is associated with mutations in C10orf11. The isoform 1 open reading frame encodes a 226 amino acid protein containing a leucine-rich repeat. The function of the protein is unknown but is thought to play a role in melanocyte differentiation.

**III. MUTATIONS AND OCULOCUTANEOUS ALBINISM**

Most mutations described associated with OCA have been single base substitutions that result in either amino acid substitutions, RNA splicing abnormalities or premature stop codons (nonsense or frameshift mutations). New evidence has shown that larger deletions and chromosome rearrangements are also important mechanisms for mutating genes associated with OCA. Deletions or duplications are thought to account for over 5% of mutations associated with OCA.

It is important to note that all individuals carry 4-5 abnormal genes among the 30,000 or so genes that we have. Parents who are close relatives (consanguineous) have a higher chance than unrelated parents to both carry the same abnormal gene, which increases the risk to have children with a recessive genetic disorder.Four genes have been identified that are associated with different types of OCA. Each of these genes is important in the production of melanin that takes place in cells called melanocytes that are located in the skin, hair follicle and iris and retina of the eye. In the case of skin and hair pigmentation, the melanocyte transfers the melanin pigment to the keritinocyte and make up skin and hair.

OCA1 is associated with abnormalities (mutations) in the tyrosinase (TYR) gene. The TYR gene is responsible for the production of the enzyme tyrosinase which is responsible for the first step in the formation of melanin pigment. Some TYR mutations result in the production of a nonfunctioning tyrosinase enzyme and no melanin pigment is formed. This type of OCA1 is called OCA type 1A (OCA1A). Other TYR mutations result in the production of a tyrosinase enzyme with reduced function so that a reduced amount of melanin pigment is formed. This type of OCA1 is called OCA type 1B (OCA1B). In the case of OCA1B, melanin pigment will accumulate with time.

OCA2 is associated with mutations in the OCA2 gene (also called the P gene). The OCA2 gene is responsible for production of the OCA2 protein. The precise function of the OCA2 protein is unknown, but it is thought to be important in regulating the movement of the substrate tyrosine into the melanosome as well as regulating the internal environment of the melanosome.

OCA3 is associated with mutations in the tyrosinase related protein 1 (TYRP1) gene. This gene is responsible for the production of tyrosinase-related protein-1, an enzyme, like tyrosinase, that is involved in the production of melanin. The TYRP1 enzyme is part of a gene family that includes tyrosinase and the tyrosinase related protein-2 (TYRP2), all of which are enzymes involved in melanin biosynthesis. The TYRP1 enzyme is responsible for later steps (after the initial tyrosinase step) in melanin pigment production.

OCA4 is associated with mutations in the SLC45A2 gene (also called the MATP). The SLC45A2 gene is responsible for the production of this membrane associated transporter protein. The precise function of this protein is unknown but it is required for the normal production of melanin by the melanocyte.

It is important to note that all individuals carry 4-5 abnormal genes among the 30,000 or so genes that we have. Parents who are close relatives (consanguineous) have a higher chance than unrelated parents to both carry the same abnormal gene, which increases the risk to have children with a recessive genetic disorder.

**IV. SYMPTOMS AND CAUSES**

* pale skin
* hair that is very light blonde, brown, or reddish
* eyes that are pink, light blue, green, gray, or light brown
* eyes that are sensitive to light
* a “lazy eye” (called strabismus)
* back and forth movement of the eyes (called nystagmus)
* vision problems

Albinism that only affects the eyes is called ocular albinism. Sometimes albinism can be part of other medical conditions.

**V. DIAGNOSIS**

OCA type 1 can be distinguished from OCA types 2 and 3 on the basis of subtle clinical differences and the presence or absence of [tyrosinase](https://www.sciencedirect.com/topics/medicine-and-dentistry/tyrosinase) activity. OCA type 1 is the tyrosinase-negative variant and can be diagnosed prenatally with a fetal [skin biopsy](https://www.sciencedirect.com/topics/medicine-and-dentistry/skin-biopsy) specimen (Holbrook et al, 1993). It results from any of several defects in the tyrosinase gene (Tomita, 1994). In type 2 and type 3 OCA, tyrosinase activity is positive. Genetic testing of tyrosinase and *P* genes may be necessary to distinguish OCA type 2 from type 3 (King et al, 2003). Oculocutaneous [albinism](https://www.sciencedirect.com/topics/medicine-and-dentistry/albinism) should be distinguished from simple [ocular albinism](https://www.sciencedirect.com/topics/medicine-and-dentistry/ocular-albinism), which has sex-linked, [autosomal dominant](https://www.sciencedirect.com/topics/medicine-and-dentistry/autosomal-dominant-inheritance), and [autosomal recessive](https://www.sciencedirect.com/topics/medicine-and-dentistry/autosomal-recessive-inheritance) forms.

**VI. Treatment**

**a) Eye care.** This includes receiving an eye exam at least every year by an ophthalmologist. You'll likely need prescription lenses to help with visions problems. Although surgery is rarely part of treatment for eye problems related to albinism, your ophthalmologist may recommend surgery on eye muscles to reduce nystagmus. Surgery to correct strabismus may make the condition less noticeable.

**b) Skin care and prevention of skin cancer.** This includes receiving a skin exam at least every year to screen for skin cancer or spots that can lead to cancer. An aggressive form of skin cancer called melanoma can appear as pink or red moles or growths. Moles or growths, with or without color — especially ones that are pink or red and keep changing — should be checked by a skin specialist right away

**VII. LIFESTYLE AND HOME REMEDIES**

You can help your child learn self-care practices that should continue into adulthood:

* **Use low vision aids,** such as a hand-held magnifying glass, a telescope or a magnifier that attaches to glasses. Another aid is a tablet connected to a digital whiteboard in the classroom. This is an interactive electronic board with a touch screen.
* **Always use sunscreen** with a sun protection factor (SPF) of 30 or greater that protects against both UVA and UVB light.
* **Strictly avoid high-risk or lengthy sun exposure.** Examples include being outside for long periods of time or in the middle of the day, at high altitudes, on or near water, and on sunny days with thin cloud cover.
* **Wear protective clothing,** including clothes with color. Examples include long-sleeve, collared shirts, long pants and socks; broad-brimmed hats; and special UV-protection clothing.
* **Protect eyes** by wearing dark, UV-blocking sunglasses. Another option is transition lenses called photochromic lenses, which darken in bright light.

**VIII.** **CONCLUSION**

[Albinism](https://www.sciencedirect.com/topics/medicine-and-dentistry/albinism) refers to a group of genetic conditions that are characterized by reduced [melanin](https://www.sciencedirect.com/topics/nursing-and-health-professions/melanin) levels leading to [hypopigmentation](https://www.sciencedirect.com/topics/medicine-and-dentistry/hypopigmentation) of the eyes, hair, and skin, and importantly, all affect vision. Simple or nonsyndromic forms of [albinism](https://www.sciencedirect.com/topics/medicine-and-dentistry/albinism) affect [melanosomes](https://www.sciencedirect.com/topics/medicine-and-dentistry/melanosome) only, whereas complex or syndromic forms of albinism include systemic features caused by disturbances in both melanosomes and other intracellular organelles.

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