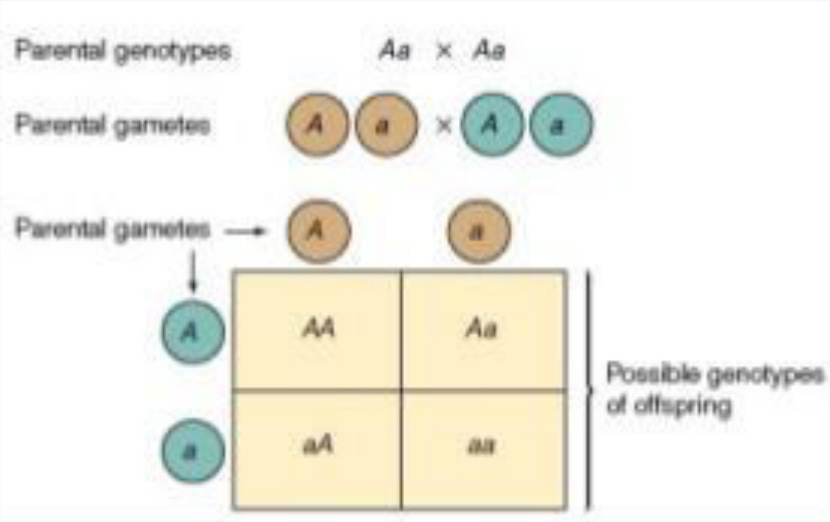
# Albinism

# Albinism

- Albinism is an ***inherited genetic*** condition. Most child( 1in every 75 people) are carriers for albinism. pigment needed for various functions – including vision are absent in albino.
- Albinism is an autosomal recessive disorder. This means that the person with albinism must receive one copy of the mutated gene from their mother, and one from their father.

# Phenotypically Normal Parents, Both Carriers of the Albinism Allele




- Offspring:
- Homozygous dominants (AA) with normal phenotype, 25%
- Heterozygotes, (carriers) (Aa) with normal phenotype, 50%
- Homozygous recessives (aa) with albinism, 25%.

- Melanins are biological polymers made in the melanocytes located in the hair follicles, iris of the eye, retinal and inner ear. The synthesis of melanin involves tyrosinase enzymes a rate limiting step in the syntheses of melanin, which serves a protective function for the skin and eye.

- albinism is caused by mutations in seven genes as a result of recessive inheritance of autosomal chromosomes.
- These genes are responsible for different types albinism.
- It is a genetic mutation due to lack of melanin pigment in the skin, hair, and eye .
- If the person has only one copy of the mutated gene they won't have albinism.

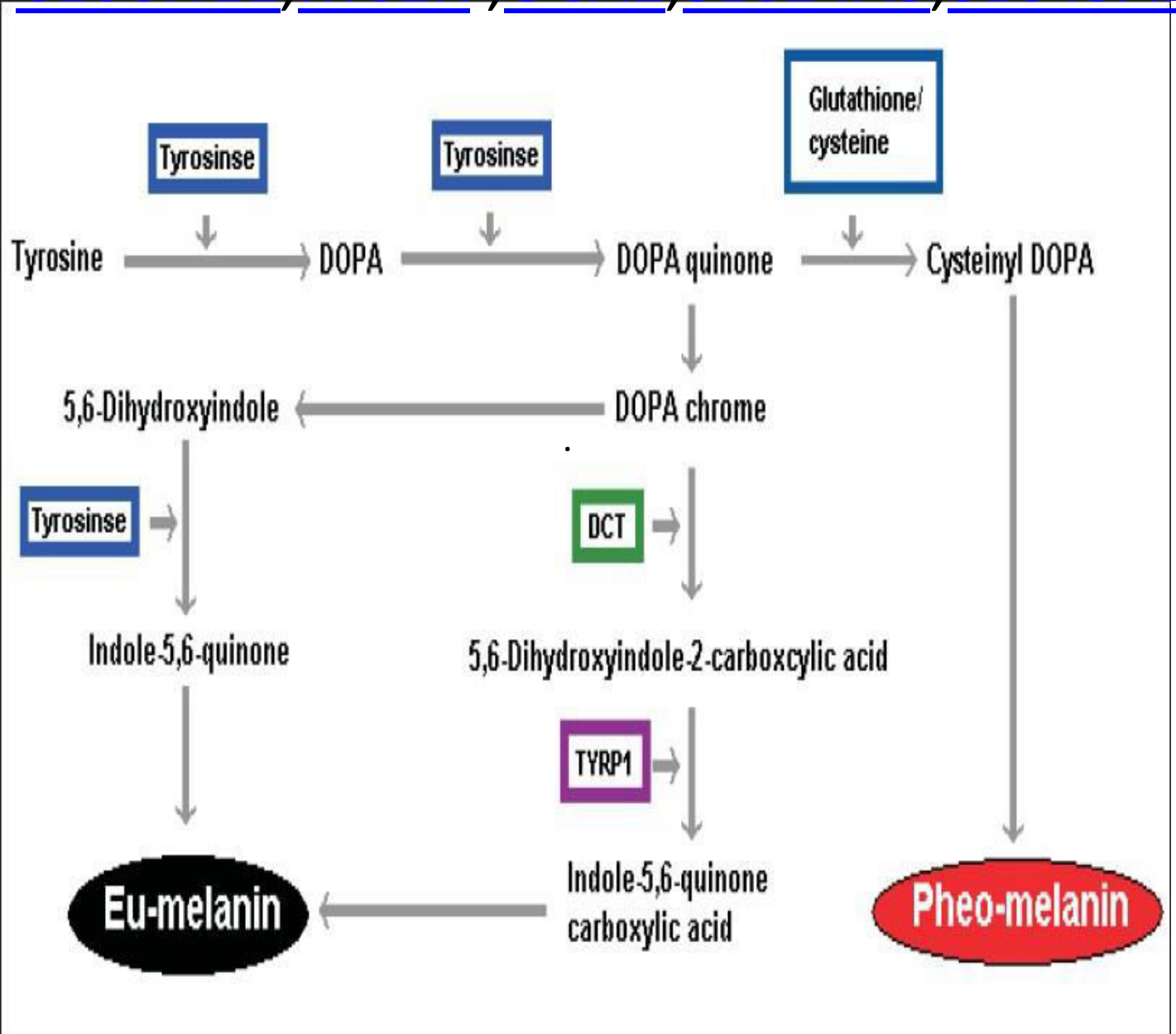
| Human Locus |
| --- |
| TYR |
| OCA2 |
| TYRP1 |
| SLC45A2 |
| HPS1 |
| AP3B1 |
| HPS3 |

# five types of albinism

- five types of albinism that can be inherited include:
- Oculocutaneous albinism,
- Ocular type1 albinism
- Hermansky-Pudlak syndrome,
- Chediak-Higashi syndrome, and
- X-linked ocular albinism which is a sex-linked type of albinism.

genes associated with oculocutaneous albinism

C10orf11,MC1R ,OCA2,SLC24A5,SLC45A2,TYR,TYRP1

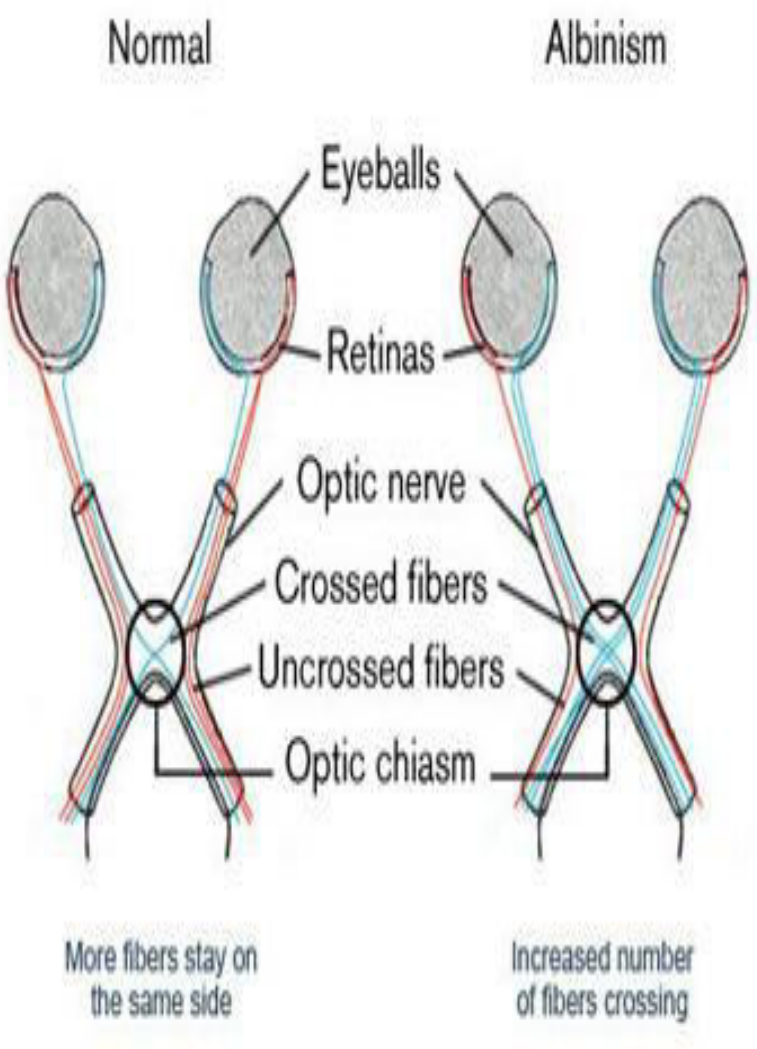


| Type of Albinism | Human Locus | OMIM Link | Link to Table of Mutations and Polymorphisms | Map of Mutation Locations |
|---|---|---|---|---|
| Oculocutaneous albinism type 1 (OCA1) | *TYR* | 203100 (OCA1A<br>606952 (OCA1B) | Mutations and Polymorphisms of TYR | Mutation locations for TYR |
| Oculocutaneous albinism type 2 (OCA2) | *OCA2* | 203200 | Mutations and Polymorphisms of P | Mutation locations for P |
| Oculocutaneous albinism type 3 (OCA3) | *TYRP1* | 203290 | Mutations and Polymorphisms of TYRP1 | Mutation locations for TYRP1 |
| Oculocutaneous albinism type 4 (OCA4) | *SLC45A2* | 606574 | Mutations and Polymorphisms of SLC45A2 | Mutation locations for SLC45A2 |
| Hermansky-Pudlak Syndrome type 1 (HPS1) | *HPS1* | 203300 | Mutations and Polymorphisms of HPS1 | Mutation locations for HPS1 |
| Hermansky-Pudlak Syndrome type 2 (HPS2) | *AP3B1* | 603401 | Mutations and Polymorphisms of ADTB3A | Mutation locations for ADTB3A |
| Hermansky-Pudlak Syndrome type 3 (HPS3) | HPS3 | 606118 | Mutations and Polymorphisms of HPS3 | |
| Hermansky-Pudlak Syndrome type 4 (HPS4) | HPS4 | 606682 | | |
| Chediak-Higashi Syndrome | *LYST* | 214500 | Mutations and Polymorphisms of LYST | Mutation locations for LYST |
| Ocular Albinism type 1 | *GPR143* | 300500 | Mutations and Polymorphisms of GPR143 | Mutation locations for GPR143 |

## Oculocutaneous Albinism Genetics

| Type | Gene | Location* |
|---|---|---|
| Type 1 | TYR | 11q14-q21 |
| Type 2 | OCA2 | 15q11.2-q12 |
| Type 3 | TYRP1 | 9p23 |
| Type 4 | SLC45A2 | 5p13.3 |
| Type 2 Modifier | MC1R | 16q24.3 |

* indicates chromosome number and gene location




- albinism generally leads to some type of vision problems for those affected. Many have very poor vision and may be classified as *legally* blind. Impaired vision results from the **retina not completely developing**; **additionally, nerve connections are irregular between the eye and brain**, and these eye problems often lead to the initial diagnosis of albinism.

# *TYRP1* gene

- The *TYRP1* gene provides instructions for making an enzyme called tyrosinase-related protein 1. This enzyme is located in melanocytes, *TYRP1* may help stabilize tyrosinase & also determine the shape of melanosomes

# Oculocutaneous albinism

- The first type involves a gene mutation on **chromosome 11**.
- People with this type of albinism will have milky white skin, white hair, and blue eyes at birth.
- Some people with this disorder may begin to produce melanin during early childhood or in their teenage years, which causes their pigmentation to change.

# The appearance of patient of Oculocutaneous albinism

- This may cause their hair to change to a golden blond or a brown.
- The skin colour usually won't change, but they **may get somewhat of a tan.**
- The eyes may also change colour and lose some of their translucency.
- Other people with this type of albinism won't experience changes in pigment.

# Tyrosinase

- Tyrosinase is responsible for the first step in melanin production.
- It converts a protein building block (amino acid) called tyrosine to another compound called dopaquinone.
- A series of additional chemical reactions convert dopaquinone to melanin in the skin, hair follicles, the colored part of the eye (the iris), and the retina.

# *TYR* gene

- The *TYR* gene provides instructions for making an enzyme called tyrosinase. This enzyme is located in melanocytes, which are specialized cells that produce a pigment called **melanin**.
- Melanin is the substance that gives skin, hair, and eyes their color. Melanin is also found in the light-sensitive tissue at the back of the eye (the retina), where it plays a role in normal vision.

- *TYR* gene provides instructions for making an enzyme called tyrosinase.
- ***TYRP1*** gene provides instructions for making an enzyme called tyrosinase-related protein 1,
- ***TYRP1*** may also help to stabilize tyrosinase & also determine the shape of melanosomes
- ***OCA2*** gene make P protein may also help regulate the relative acidity (pH) of melanosomes
- **The *SLC45A2*** gene (also called *MATP*) provides instructions for making a protein that is located in specialized cells called melanocytes.

# Types of albinism:

- Eye color in particular is a complex trait
- **Type 1 or OCA 1A**
- **Type 2** (OCA2 or P gene albinism)
- **Type 3** Tyrosinase-related protein-1 gene (TYRP1) or OCA3 Oculocutaneous albinism (OCA3)
- **Type 4** Oculocutaneous albinism (OCA4)
- **X-linked ocular albinism gene and OA1**

# Oculocutaneous Albinism

## autosomal recessive pattern,

- **Oculocutaneous Albinism (OCA)** affects the eyes, hair and skin and includes several different forms.
- The first form, **OCA1** involves the tyrosinase enzyme, which converts tyrosine (an amino acid) into melanin. Melanin is a chemical that colors our skin, eyes and hair

# Type 1 or OCA 1A

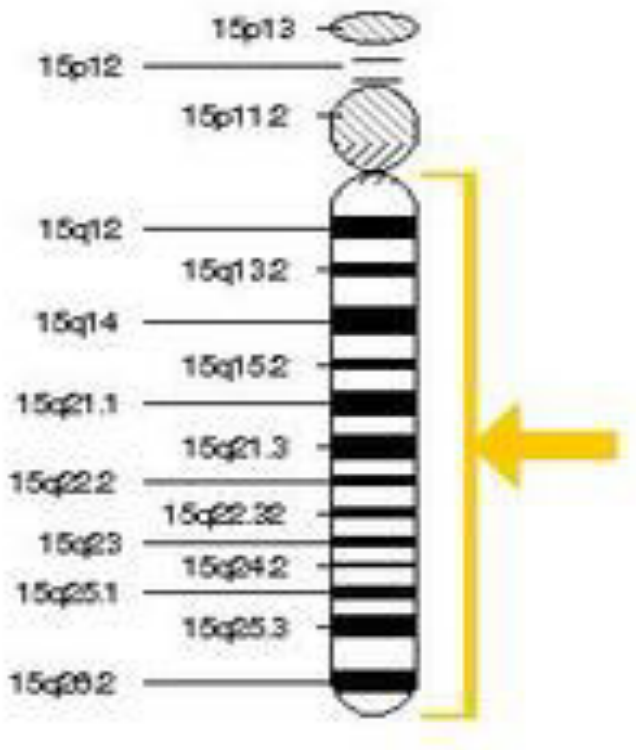
- defect in Tyrosinase enzyme which leads to **inactive enzymes and no melanin produced**,: characterized by white hair, very pale skin, and light-colored irises. In **OCA 1B,** the **enzyme is minimally active and a small amount of melanin is produced**, leading to hair that may darken to blond, yellow/orange or even light brown, as well as slightly more pigment in the skin.

# OCA1 includes two sub-groups:

- **OCA1a:** Those with this type of albinism have ***no pigment*** and ***no active tyrosinase***
- **OCA1b:** Those with this type of albinism have ***some residual tyrosinase activity*** and so have ***some pigment***. Although they have decreased pigmentation at birth, it may increase slightly throughout their lives. People in this group may even have the ability to sun tan.

# **Type 2** (OCA2 or P gene albinism)

- Chromosome 15: base pairs 27,754,874 to 28,099,336. The cytogenetic location is on the long q arm.



# **Type 2** (OCA2 or P gene albinism)

- results from a genetic **defect in the P protein** that helps the tyrosinase enzyme to function. Individuals with OCA2 make a minimal amount of melanin pigment and can have hair color ranging from very light blond to brown. Typically less severe than type 1. It occurs more frequently in African-Americans, Africans and some Native American groups

# OCA2 gene mutation

## p-protein involved in melanin production

- Another form of OCA, **OCA2**, affects the p-protein, another protein involved in melanin production. It is much more common in persons of ***African descent***.
- People in this group have ***some pigment***, but **typically do not tan.**

# *OCA2* gene make P protein.

- P protein is located in melanocytes, which are specialized cells that produce a pigment called melanin. P protein transport molecules into and out of structures called melanosomes

## **Type 3** Tyrosinase-related protein-1 gene (TYRP1) or OCA3 Oculocutaneous albinism (OCA3)

- is rarely described and results from a genetic defect in **TYRP1, a protein related to tyrosinase**. Individuals with OCA3 can have substantial pigment. It also includes a form of albinism , which usually affects dark-skinned people. Affected people have reddish-brown skin, reddish hair, and hazel/brown irises. It is often associated with milder eye problems.

# *SLC45A2* gene
# solute carrier family 45 member 2

- The *SLC45A2* gene (also called *MATP*) provides instructions for making a protein that is located in specialized cells called melanocytes.
- These cells produce a pigment melanin.
- Studies suggest that certain common variations (polymorphisms) in the *SLC45A2* gene may be associated with normal differences in skin, hair, and eye coloring.

- Although the exact function of the SLC45A2 protein is unknown, it is likely involved in the production of melanin.
- This protein probably transports molecules necessary for the normal function of melanosomes, which are the structures in melanocytes where melanin is produced.

# *Type2 modifier MC1R* gene

- Alterations in the *MC1R* gene can change the appearance of people with oculocutaneous albinismtype 2.
- This gene helps regulate melanin production and is responsible for some normal variation in pigmentation.

# *OCA2* and *MC1R* genes

- People with genetic changes in both the *OCA2* and *MC1R* genes have many of the usual features of oculocutaneous albinism type 2, including light-colored eyes and vision problems; however, they typically **have red hair** instead of the usual yellow, blond, or light brown hair seen with this condition.

# **Type 4** Oculocutaneous albinism (OCA4)

- results from a genetic defect in the **SLC45A2 protein that helps the tyrosinase enzyme to function.**Individuals with OCA4 make a minimal amount of melanin pigment similar to persons with OCA2. It has signs and symptoms similar to those seen with type 2. It occurs more frequently in Japanese and Korean origins

# OCA4 with SLC45A2 gene

- Yet another form of OCA, **OCA4**, is clinically indistinguishable from OCA2.
- However, it involves the SLC45A2 gene, which produces another protein involved in melanin production.

# Hermansky-Pudlak Syndrome (HPS)

- **Hermansky-Pudlak Syndrome (HPS)** is a rare type of albinism, which has an increased incidence among people of Puerto Rican descent.
- It may involve bleeding disorders, bruising, lung problems and intestinal disorders.

# Hermansky-Pudlak syndrome

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|---|---|---|---|---|
| Hermansky-Pudlak Syndrome type 1 (HPS1) | *HPS1* | 203300 | Mutations and Polymorphisms of HPS1 | Mutation locations for HPS1 |
| Hermansky-Pudlak Syndrome type 2 (HPS2) | *AP3B1* | 603401 | Mutations and Polymorphisms of ADTB3A | Mutation locations for ADTB3A |
| Hermansky-Pudlak Syndrome type 3 (HPS3) | HPS3 | 606118 | Mutations and Polymorphisms of HPS3 | |
| Hermansky-Pudlak Syndrome type 4 (HPS4) | HPS4 | 606682 | | |

# Hermansky-Pudlak syndrome

- Hermansky-Pudlak syndrome is a rare form of the disorder.
- The second type involves a gene mutation on **chromosome 15**.
- **It involves a mutation in one of at least eight genes associated with this syndrome.**
- The signs of this syndrome are similar to those of Oculocutaneous albinism, but the **person also develop a bleeding disorder, as well as lung and bowel diseases.**

*HPS1*

*AP3B1*

HPS3

HPS4

# The appearance of patient of Hermansky-Pudlak syndrome

- This type is more common in Sub-Saharan Africans, African-Americans and Native Americans than in other population groups.
- These people may have yellow, auburn, ginger, or red hair.
- The eyes can be blue-gray or brown.
- The skin is white at birth. The skin colour is generally a little lighter than the family's colouring. The skin may be able to develop **freckles, moles or lentigines, if exposed to the sun.**

# Chediak-Higashi Syndrome

- **Chediak-Higashi Syndrome** is another rare form of albinism. It is characterized by an abnormality in certain types of white blood cells, lowering resistance to infection.

# Chediak-Higashi syndrome

- The third and rarest type involves a gene mutation on **chromosome 9**. This type is mostly found in black South-Africans.
- These people usually have reddish-brown skin, ginger or reddish hair, and hazel or brown eyes.
- Chediak-Higashi syndrome is also a rare form of albinism that is involved with a mutation in the **LYST gene**.
- The appearance of someone with this disorder is similar to Oculocutaneous albinism.
-

# The appearance of patient of Chediak-Higashi syndrome

- The skin will usually be creamy white to grayish.
- **People with this syndrome will have problems with their white blood cells. This makes them more susceptible to infections, and makes it harder for them to fight them off.**

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|---|---|---|---|---|
| Chediak-Higashi Syndrome | *LYST* | 214500 | Mutations and Polymorphisms of LYST | Mutation locations for LYST |

# Griscelli Syndrome

- **Griscelli Syndrome** is an extremely rare type of albinism. In fact, there are only 60 known cases worldwide. Like Chediak-Higashi Syndrome, it involves immunodeficiency and may also have associated neurological problems. You can learn more at emedicine.com/derm/topic926.htm.

# Ocular Albinism

## X-linked chromosomal inheritance

- **Ocular Albinism (OA)** affects only the eyes, not the skin or hair. It results from an X-linked chromosomal inheritance and so occurs mostly in boys.
- X-linked ocular albinism is the sex linked form of albinism. This form of albinism mostly occurs in males, and is a gene mutation found on the X chromosome.

# The appearance of patient of X-linked ocular albinism

- People with this type also have the same functional and developmental vision problems as other types of albinism.
- The hair, skin, and eye colour are usually in the normal range or they are slightly lighter than other people in the family

| Type of Albinism | Human Locus | OMIM Link | Link to Table of Mutations and Polymorphisms | Map of Mutation Locations |
|---|---|---|---|---|
| Ocular Albinism type 1 | GPR143 | 300500 | Mutations and Polymorphisms of GPR143 | Mutation locations for GPR143 |

# X-linked ocular albinism gene and OA1

- (affects just the eyes),HPS gene/ Hermansky-Pudlak syndrome, and CHS gene (CHS1)/ Chediak-Higashi syndrome have characteristics that overlap with oculocutaneous albinism

- Those affected by albinism may also experience **vision defects, higher susceptibility to sunburn and skin damage due to UV rays, and dampened immune systems**.

mutations in several genes

**OCA1** *TYR*, *OCA2*, *TYRP1*, and *SLC45A2*