

What Is Ocular Albinism?

Ocular Albinism (also known as OA1 or Nettleship-Falls Ocular Albinism) is an X-linked recessive condition that results from the mutation of the *GPR143* gene and is usually associated with less than normal visual acuity. The *GPR143* gene creates a signaling protein that plays a key role in the development of the eye. When the signaling does not occur, the ocular features like nystagmus, foveal hypoplasia, and others described below can happen. This is why individuals with ocular albinism (OA) and oculocutaneous albinism (OCA) have the same vision symptoms, but different levels of pigment in their hair and skin. Ocular Albinism may not have the pigimentary changes in the skin or hair like oculocutaneous albinism because melanin production is not affected by the *GPR143* gene.



Three year old with OA on his first day of preschool.

CROSS SECTION OF THE EYE

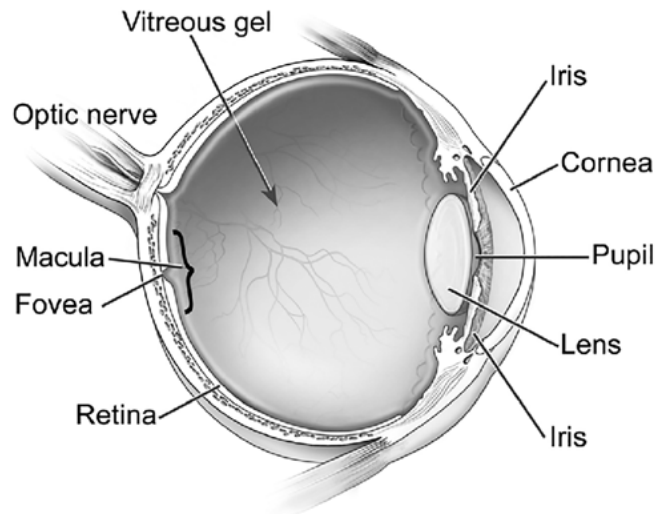


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Vision and OA

Vision (the quality of eyesight) can be affected by OA in several ways. It is important to remember that the eyesight of each person with OA, even in the same family, may be affected differently. The visual system is made up of many different elements, each of which may be altered to different degrees. The characteristics of OA are discussed below, including nystagmus, iris transillumination, photodysphoria, underdeveloped macula and fovea, and a misrouting of the optic nerve fibers back to the brain.

Nystagmus

The earliest and sometimes the most noticeable characteristic is nystagmus. 'Nystagmus' is the medical term for a constant, persistent, involuntary movement of the eyes, typically horizontally back and forth. For people with OA, nystagmus is almost never present at birth but typically appears four to twelve weeks after birth. The speed and amplitude of nystagmus varies among individuals, even in the same family, and

will generally diminish slowly as the person grows into their teenage years, but it never disappears. The brain does not perceive the movement but will see a less-clear image due to the constant movement of the image on the retinas. When looking at a target or object, the eye movements may shorten in length and become quicker. Sometimes, a person will assume an abnormal head position, such as a face turn or a head tilt, because the nystagmus dampens in that position and therefore the brain gets a clearer and more stable image. The position of the eyes where the nystagmus is minimized is called a “null point.”

Iris Transillumination

The reduced presence of pigment affects the ocular system for people with OA in several ways, although exactly why these changes occur are not fully understood. The iris (the colored structure in the front part of the eye that functions like the shutter opening in a camera) has a single layer of pigment-containing cells on the back side. Normally, this layer acts like a blanket and keeps light from coming through the iris tissue, except through the pupil, which lets the image through to the retina. With OA, the amount of pigment in the cells in that ‘blanket’ is reduced, which then permits light to come through the iris tissue and causes glare to scatter into the eye. This is called ‘iris transillumination’ and can be seen during an examination by an ophthalmologist or an optometrist with a microscope called a ‘slit lamp.’ As a result of iris transillumination, people with OA can be sensitive to bright light and glare, sometimes called ‘photophobia,’ which means “painful aversion to bright light.” A more accurate term is ‘photodysphoria,’ meaning “discomfort in bright light,” since the glare may be uncomfortable but does not cause pain.

HEALTHY RETINA

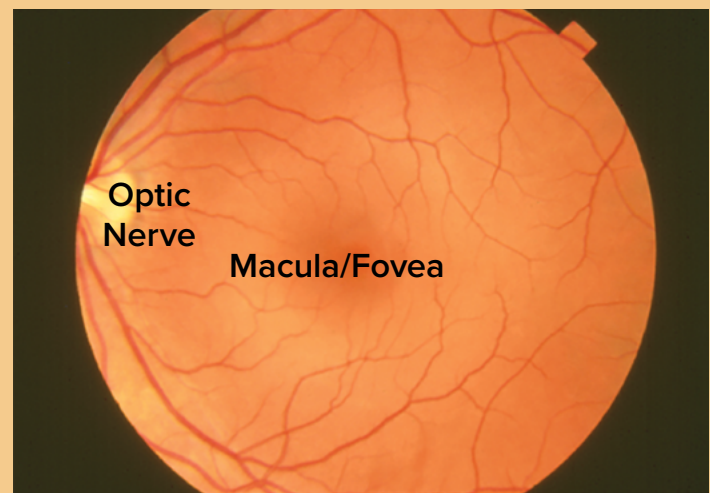


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Macula and Fovea

The center parts of the retina that are responsible for detailed vision (macula and fovea) have reduced amount of pigment, which means less light information is transmitted from the retina to the brain. The result of an underdeveloped macula and fovea, also called foveal hypoplasia, results in reduced perception of fine details. The brain is receiving less data to render a sharp and complete image.

Optic Nerve and Strabismus

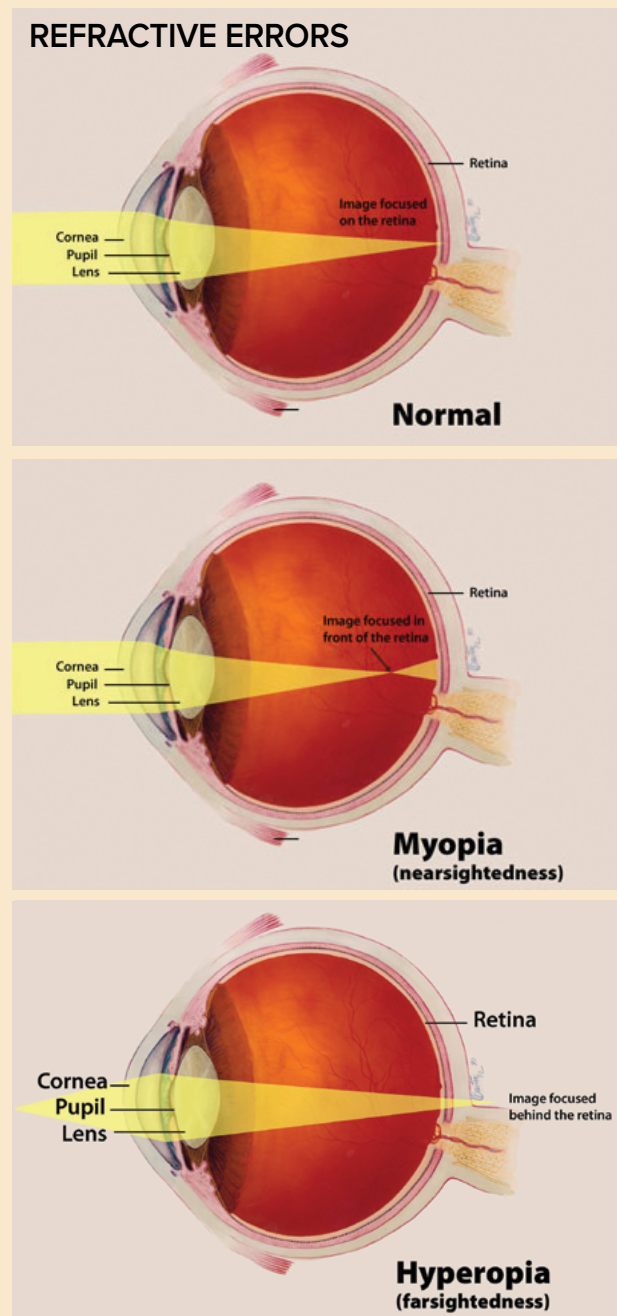
Millions of nerve fibers pass through the optic nerves to various parts of the brain. Although it is not understood why, it is well-established that the nerve fibers do not follow the same routes into and through the brain as they do in an individual without albinism. As a result of this misrouting of the information to the brain, people with OA often develop ‘strabismus,’ which is a misalignment of the eyes, meaning the eyes are not straight and parallel to one another. This creates issues with depth perception. When the eyes are not aligned on the same object at the same time, they cannot transmit simultaneous, overlapping, cohesive 3D images to the brain. Refractive errors are also common in people with OA and vary widely between individuals.

Refractive Errors

Refractive errors result from changes in the shape and length of the eye, cornea, and lens. These variations affect how and where light is focused onto the retina in the back of the eye. To achieve a clear image, all rays of light must be bent or focused (refracted) exactly on the same plane on the retina at the correct distance so that the entire “picture” is in focus for 360 degrees. Glasses can be prescribed to correct the way light enters the eye and therefore render a clear image. Nearsightedness (myopia) means that the eye sees things at near better than at a distance (that is, that the eyes “have near sight”). Far-sightedness (hyperopia) means that the light rays are coming into focus behind the retina, and therefore the eye is doing excessive “focusing” to bring the image forward onto the retina. Astigmatism is a refractive error related to the combined shapes of the cornea and lens. Since many human eyes are not perfect spheres, light rays are not focused on the same plane on the retina. Glasses can be used to bring the incoming light onto the retina in a single flat plane to give the best possible image.

Treatment

For a person with OA, the use of prescription glasses may help to correct the refractive error and to improve visual acuity. Glasses do not change the presence or severity of nystagmus, reduction of pigment in the iris and retina, or misrouting of the optic nerves. While physicians cannot repair the underdevelopment of the macula and fovea, they can compensate to get the image(s) onto the retina sharp and clear. Sunglasses and tinted prescription lenses can be helpful to reduce glare and discomfort in bright light.



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Acuity

A person's quality and experience of vision (“acuity”) can vary greatly. Two individuals can have the same visual impairment but experience their visual world differently. Visual acuity is a measurement used during an ophthalmologist or optometrist's examination to quantify a person's ability to perceive details. It is presented as a fraction with 20 as the numerator and effectively compares what a “standard-sighted person” should be seeing

at 20 feet. A person whose vision is “20/20” can see at 20 feet what the standard person can see at 20 feet. On the other hand, a person with 20/200 visual acuity can perceive the level of detail at 20 feet that a standard person could resolve at 200 feet. The visual acuity of a person with OA can range from 20/40 to 20/200 (or, uncommonly, worse) with best possible correction in either glasses or contact lenses.

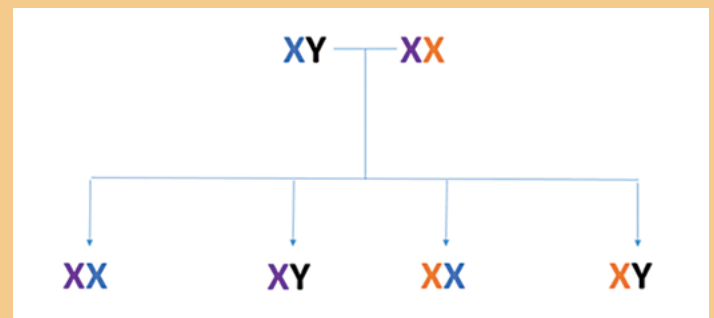
Family Connection

Ocular albinism is a genetic condition. Genes are grouped into chromosomes and humans have 23 pairs of chromosomes. A person gets one chromosome in the pair from each parent. The last pair is considered our sex chromosomes as the 23rd pair will differ between males and females. Biological female sex is determined by having two X-chromosomes. Biological male sex is determined by having an X chromosome and a Y chromosome. The genes on the X and Y chromosome differ and lead to different sexual development of a baby in pregnancy. Mothers can only pass on an X chromosome to her children. Fathers have a 50% chance to pass on their X chromosome or Y chromosome to their children, therefore determining the biological sex of the baby.

Traits are the physical expressive of genes and they may be either dominant or recessive. A dominant trait will “override” or predominate over a recessive trait and become the selected expression of that gene. For example, the genetic trait for curly hair is dominant and straight hair is recessive. Someone who inherits the gene for curly hair will always have

curly hair, even if paired with the second copy of a gene for straight hair.

Example of chromosome combinations possible from a set of male and female parents:



Genes located on the X chromosome follow an X-linked inheritance pattern. Symptoms of an X-linked inheritance pattern affect males and females differently. Males are more classically affected with X-linked conditions. Females with a pathogenic variant in a gene located on one of their X-chromosome are considered carriers. Carrier females can have a wide spectrum of symptoms depending on the gene and condition. Most carrier females of an X-linked condition are asymptomatic or only have mild symptoms.

Ocular albinism is an X-linked condition as there is only one gene, *GPR143*, that can cause the condition. The *GPR143* gene is located on the X chromosome. Males will experience the



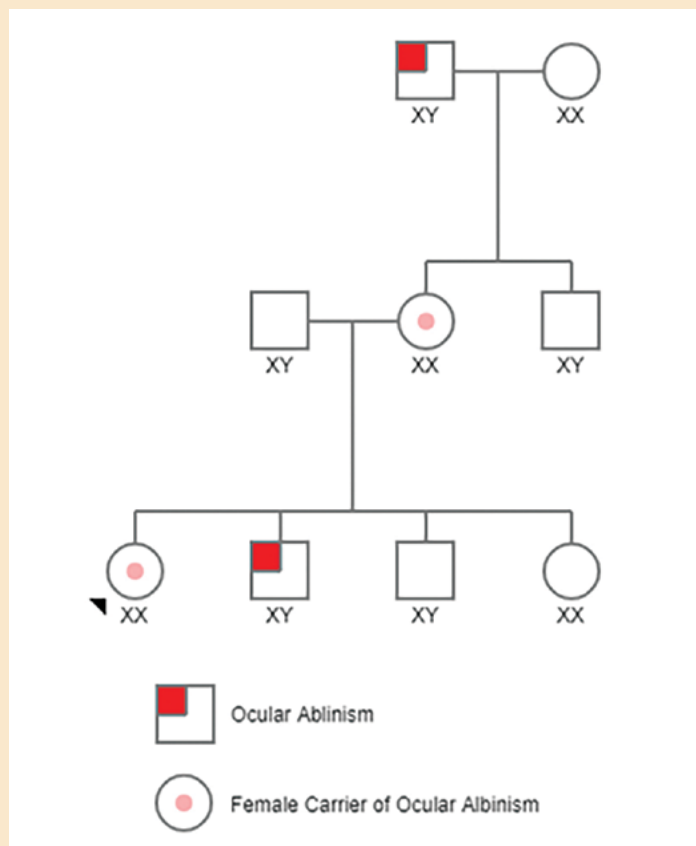
Infant with OA.



Uncle and nephew with OA.

vision symptoms of OA described above since males have only one copy of the *GPR143* gene. Females have two copies of the *GPR143* gene, so depending on what X chromosome is being expressed in the eye, have mild signs or none at all. OA is a “recessive” trait, which means the carrier female will not have reduced visual acuity or many of the associated features of OA, because she has a second X-chromosome that includes a “normal” copy of *GPR143* gene that does not give rise to the trait. However, most female carriers have minor features in their irises and retinas. Minimal iris transillumination defects can be observed during an eye examination. The retina may appear to have irregular patches or blotches of increased pigmentation, often called “mottling,” because different clusters of those cells contain more than or less than normal amounts of pigment.

Here is a sample family tree to demonstrate how OA1 can be passed down through generations:



HEALTHY RETINA

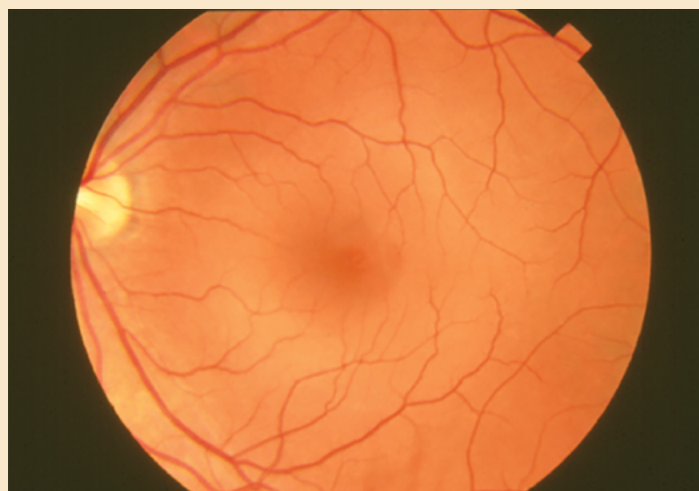


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EXAMPLE OF MOTTLING IN A FEMALE CARRIER OF OA1



Image Credit: image of a mother's retina taken by an ophthalmologist.

How is OA diagnosed?

The only way to diagnose OA accurately is a genetic test, confirming a pathogenic variant in the *GPR143* gene. Presence of low vision and/or nystagmus in male family members along with the ocular features mentioned above during an eye examination may suggest the possibility of OA, but does not confirm the diagnosis. Oculocutaneous albinism (OCA) can present with a spectrum of pigmentary levels in the skin and hair. Some individuals with OCA who have mild pigmentary changes

in their skin and hair but have low vision might receive a diagnosis of OA. However, the genetic cause of OCA is different; seven genes that play a key role in creating melanin are the cause. OCA is also inherited in a recessive pattern when both copies of the gene (maternal and paternal) need to have a pathogenic variant before someone will experience symptoms of the condition. Panel-based genetic testing including the genes associated with OCA and the *GPR143* gene can be helpful in understanding if a person has OCA or OA. Genetic testing panels can also include genes that can cause syndromic forms of albinism like Hermansky-Pudlak Syndrome as well as genes associated with isolated nystagmus or foveal hypoplasia. OA is considered “rare,” though no realistic evaluations of large populations are available. Some guesses range between 1 person in 20,000 to 1 in 50,000 in the general population. There are multiple genetic laboratories who have this type of genetic testing available. If you are interested in genetic testing for albinism, reaching out to your ophthalmologist, primary care provider, or medical geneticist is recommended to start the conversation.

Support

NOAH welcomes people with OA, their caregivers and their families. While they have a lot in common with people with albinism, they also have a unique experience with the familial and genetic component and not looking quite like people with hypopigmentation. NOAH is in the process of developing a greater presence and awareness of people with OA. New caregivers are encouraged to sign up for a Parent Liaison and to join Parent Connections for OA.

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Seven year old with OA on a family camping vacation.



Photos above courtesy of Positive Exposure, Rick Guidotti

NOAH envisions a world where people with albinism are empowered to be fully functioning members of society, where barriers and the stigma of difference no longer exist, and where people with albinism have a quality of life that is rewarding, dignified and fulfilling. The organization hosts biennial events for our community which include a national conference on even-numbered years and family summer camp and an adults

with albinism weekend on odd-numbered years. In addition, local events are hosted by community members in many areas of the U.S. and Canada.

Visit **www.albinism.org** or more information about albinism including bulletins, events, ways to connect with the albinism community and to subscribe to NOAH's large-print quarterly magazine, *Albinism InSight*.



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