

Ocular Disease: Mechanisms and Management

Chapter 64: Color Vision Defects

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CLINICAL BACKGROUND

Key symptoms and signs

“Normal” color vision refers to the form of trichromatic color vision shared by most humans. It is mediated by three types of retinal cone photoreceptors, designated long-(L), middle- (M), and short-(S) wavelength cones. Each cone type is maximally sensitive to a different region of the visible spectrum (**Figure 1**). The neural circuitry for color vision compares the outputs of the three cone types and generates neural signals that give rise to the percepts of six basic colors: blue, yellow, red, green, black, and white, and to their mixtures. Color vision defects can either be inherited as the consequence of gene defects that affect the function of one or more cone type, or they can be acquired secondary to disease or through exposure to neurotoxins. The hallmark feature of color vision defects is a reduction in the number of different colors that are seen as distinguishable from each other. The terms *protan* and *deutan* refer to color vision defects that result from abnormalities in the L and M cones and are collectively termed red-green color vision deficiency. These are characterized by diminished sensations of red and green which translates to a difficulty with several color combinations, 1) confusion between colors in the middle-to-long wavelength region of the spectrum which include green, yellow, orange and red, particularly the pale versions of those colors and their very dark counterparts, olive, brown and brick, 2) Confusion between greenish and reddish colors, and gray, especially turquoise and gray and magenta or pink and gray 3) confusion between blue, violet and purple. The term *tritan* refers to color vision deficits that result from abnormalities in the S cones and they are characterized by diminished sensations of blue and yellow difficulty which results in confusions between dark blue and black, yellow and yellow-green and white and also confusions among colors in the short wavelength region of the spectrum, violet, purple, blue and blue-green. *Achromatopsia* refers to complete or nearly complete absence of color perception (see glossary).

Historical Development.

The mechanisms of inherited color vision defects are far better understood than are acquired defects, largely because inherited color vision deficiencies are extremely

common and they are more tractable to investigation. The first recorded description of color vision deficiency was a report by John Dalton describing his own red-green defect (1), hence *Daltonism* is the accepted term for inherited red-green color vision deficiency in many languages. Dalton hypothesized that his color vision defect was caused by blue tinted vitreous, which was disproven after his death in 1844, and in 1995, a molecular genetic study of Dalton's preserved retinas allowed the basis of his defect to be identified, which was the deletion of the gene encoding the M cone photopigment (1). Although the tendency for color vision defects to run in families and to skip generations has long been recognized, the underlying genetics has only been well characterized within the last 100 years. In the 1920s Waaler used results he collected from nearly 20,000 school children in Oslo to form the basis for his hypothesis that two separate genes on the X-chromosome – one for L cone sensitivity and another for M cone sensitivity—accounted for the inheritance patterns of normal and defective color vision (2 1457)—and over the next few decades his ideas were developed into a two locus model of red-green color vision in which a series of alleles of the L pigment gene were proposed to account for the range of protan red-green color vision defects and a separate set of alleles of the M pigment gene accounted for the range of deutan red-green defects.

The next big breakthrough in understanding the biological basis of color vision and color vision defects came when Jeremy Nathans and colleagues cloned and sequenced the genes encoding the S, M, and L cone opsins (see glossary for definition), and demonstrated that the L and M opsin genes are, in fact, adjacent on the X-chromosome. From his observations, Nathans hypothesized that color vision defects were not the result of independent mutations at separate L and M pigment gene loci as had previously believed but were instead a consequence of genetic recombination between the L and M genes. Another outcome of the tandem arrangement of the photopigment genes as observed by Nathans is that expression of both the L and M genes is controlled by a by a shared DNA regulatory element that when deleted causes blue cone monochromacy. Finally, Nathans observed that there was variability in the number of X-linked opsin gene among people with normal color vision which presumably arose from unequal crossing over between X-chromosome pigment gene arrays (3-6).

Subsequently, point mutations in the S opsin gene were found to underlie inherited tritan defects (7, 8, Gunther 2006 #1115, 9). The advent of methods for efficient genetic linkage analysis, which has been applied to families and populations affected by rod monochromacy, allowed the discovery of gene defects underlying these disorders (10).

Epidemiology

Inherited color vision defects: In the United States and Western Europe, red-green color vision defects are extremely common in both males and females, but the prevalence is about 19 times greater in males than in females because it is X-linked recessive. An estimated 1 in 12 males and 1 in 230 females is affected. The prevalence of red-green color vision defects varies with ethnicity (11). Caucasian populations in the U.S and Western Europe are reported to have the highest prevalence with about 8% of males being affected. Native Fijians have the lowest, with fewer than 1% of males affected, and African and Japanese males have intermediate frequencies with an estimated 4% of African and ~2% of Japanese males being affected (reviewed in (12)). All other color vision defects are relatively rare.

Inherited blue-yellow color vision defects affect males and females equally. Prevalence values reported in the literature range from 1 in 500 to 1 in 65,000 (10, 13). Estimating the prevalence has been challenging because most commonly used clinical color vision tests do not adequately test for color discrimination in the blue-yellow region of the spectrum. Achromotopsias are also extremely rare, and include both blue cone monochromacy and rod monochromacy. The prevalence of blue cone monochromacy, which is an X-linked trait and therefore preferentially affects males, has been estimated to be about 1 in 100,000, whereas rod monochromacy affects males and females equally, with prevalence estimates ranging from 1 in 20,000 to 1 in 50,000 (10).

Genetics

Inherited color vision defects: The vast majority of inherited color vision defects are caused by mutations that affect the expression or function of the cone photopigments.

Photopigments are comprised of a protein, termed *opsin*, attached to an 11-*cis* retinal chromophore. The cone photopigments all use the same chromophore, but different opsins. Three opsins corresponding to each cone type, L, M, and S are encoded by three genes designated OPN1LW, OPN1MW, and OPN1SW, respectively. OPN1LW and OPN1MW are located on the X-chromosome at Xq28, and OPN1SW resides on chromosome 7 at 7q32.

Blue-yellow color vision deficiency is inherited as an autosomal dominant trait caused by mutations in the OPN1SW gene. Both the common red-green color vision defects and the relatively uncommon blue cone monochromacy are X-linked, being caused by mutations and gene rearrangements of the X-chromosome opsin genes, OPN1LW or OPN1MW. For red-green defects the gene rearrangements result in the absence of one cone type, L or M, but for blue cone monochromacy the mutations result in the absence of both L and M cones. Rod monochromacies are autosomal recessive and causative mutations have been identified in the three genes: the CNGA3 and CNGB3 genes encoding the alpha and beta subunits, respectively, of the cyclic nucleotide gated ion channel that is essential for cone photoreceptors to modulate membrane potential in response to light absorption (14-18), and in the GNAT2 gene that encodes the alpha subunit of cone transducin (19). These gene defects result in the loss of function for all three cone types.

Diagnostic Work Up.

Inherited color vision defects are the result of genetic changes that are responsible for either the alteration or loss of cone photopigments. Since color vision is based on neural comparisons between different classes of cone photoreceptor, both the loss of a photopigment type and changes in the peak sensitivity of a photopigment such that there is a reduction in the differential response of two classes of cone will result in a reduced ability to distinguish colors.

There are a large number of different tests used in the diagnosis of color vision defects. Pseudoisochromatic plates are the most familiar color vision tests. The most widely used examples are Ishihara's test of color vision and the Hardy, Rand and Rittler (HRR) Pseudoisochromatic plates. These tests each consist of a book containing a series

of printed colored plates. Each plate is designed to conceal a hidden figure that can be seen by a person with normal color vision but is obscured for people with particular color vision deficiencies.

Arrangement tests, the best examples are the Farnsworth-Munsell 100 Hue Test and its abridged version the Farnsworth-Munsell Dichotomous D-15 Test, consist of a series of colored disks in which the color changes from one to the next in small steps. The caps are mixed up and the task is to “arrange” the disks “in order” so that each disk is next to the color closest to it in appearance. Color vision defects are diagnosed by the misordering of the disks.

The anomaloscope is an instrument that contains an optical system that produces two side-by-side lighted fields. One is a monochromatic amber colored field and the other is a mixture of red and green light. The task of the person being tested is to adjust the ratio of red-to-green light in the mixture until it exactly matches the amber monochromatic light. People who have inherited red-green color anomalies in which either the L or M pigment is shifted in spectral peak compared to normal will require either a higher or lower ratio of red-to-green light in the mixture. This test is extraordinarily sensitive to genetic alterations in the spectral sensitivities of the photopigments and will detect them even in individuals in which the alteration in the photopigment has little or no effect on the person’s ability to discriminate between different colors. Because of its extreme sensitivity in detecting the presence of anomalous photopigments, the anomaloscope is often referred to as the “gold standard” for diagnosing inherited red-green color vision deficiencies. However, it must be kept in mind while an abnormal result on this test does indicate a photopigment abnormality, some mild photopigment abnormalities are associated with little or no loss in color discrimination ability.

Differential Diagnosis

Each of the widely used color vision tests has its advantages and is considered to be the best test for different circumstances. Because of this, for general diagnosis of color vision defects the results from a battery of tests can provide the most complete picture from which to make a differential diagnosis. Ideally, for diagnosis of color vision

defects, one should obtain information on the “type” of problem. Is it a red-green or blue-yellow deficiency or mixed. If it is red-green, is it a “protan” or “deutan” defect. Is it a genetic disorder or is it acquired. The test should also provide information about severity. Is the person a dichromat or do they have a milder “anomalous” form of deficiency? If it is an anomalous form, is it very mild, mild, moderate or more severe? Under some conditions it is impractical to administer a battery of tests. Cole et al. (20) has recently recommended the latest edition of the Richmond HRR Pseudoisochromatic test as the “one of choice for clinicians who wish to use a single test for color vision.” It has plates for detection of both red-green and tritan defects and its classification of deutan and protan defects is useful. It is capable of grading individuals into mild, medium and strong categories. To absolutely distinguish dichromats from anomalous trichromats, the anomaloscope, the D15 or both should be used in conjunction with a pseudoisochromatic plate test.

Acquired color vision deficiencies are most reliably distinguished from inherited color vision defects using a genetic test. Presently, genetic tests are not commercially available; however, the technology exists to perform such tests because the molecular genetics of inherited color vision defects is very well understood, as will be described elsewhere in this chapter.

Treatment

Inherited color vision defects. The ability of some red-green color deficient individuals to name colors correctly and to pass standard color vision tests can be improved by placing a broadband red filter over one eye. A contact lens with a red tint, known as the X-chrom lens was developed for this purpose; however, such lenses do not cure color vision deficiency, and have been reported to cause visual distortions (21).

Gene therapy as a cure for ocular diseases has been an area of intense investigation over the last decade. Successful rescue of achromatopsia in a mouse model of rod monochromacy caused by GNAT2 mutations has been reported (22). At present, there is no cure for red-green color vision deficiency; however, in the majority of cases the cone photoreceptors are healthy and viable, and viral-mediated gene therapy is a

viable option for delivering the missing cone opsin gene to photoreceptors to rescue the defect.

Acquired color vision defects. Color vision defects acquired through exposure to toxic chemicals can frequently be treated by removing exposure to the toxin. If done soon enough, the loss in color vision is, in some cases, reversible. If a patient is to be administered drugs that have known neurotoxic effects associated with losses in color vision, a baseline color vision test should be given prior to beginning drug treatment to establish the presence or absence of an inherited color vision defect. Once drug treatment has started, patients should be monitored for changes in color vision so that drug treatment can be stopped before irreversible nerve damage occurs. Similarly, workers exposed to neurotoxins in industry should have base line color vision testing done, followed by periodic color vision testing to monitor for changes that would indicate neurotoxic effects.

PATHOLOGY

Inherited color vision defects: Red-green color vision defects are present from birth, almost always affect both eyes, are not usually accompanied by other vision problems, and are stable throughout life. As will be discussed in more detail below, under pathophysiology, red-green color vision defects are most often caused by deletions of X-chromosome opsin genes such that only one category of X-chromosome encoded opsin, L or M, is expressed. Protan defects are caused by the absence of functional L cones and protan defects are caused by the absence of functional M cones. Deutan-type defects are more prevalent than protan types, with about 6% of color deficient males having a deutan type and 2% having a protan type defect (**Table 1**). Both protan and deutan defects are sub-categorized according to the degree of color vision loss (23-25). Deutan color vision is mediated by S cones and L cones and accounts for about 6% of red-green color vision deficiency. Deutan males can either be dichromatic, having only S cones and one type of L cone, or they can be anomalous trichromats, having S cones and two different L cone subtypes (Table 1). Protan color vision is mediated by S cones and M cones, and accounts for about 2% of red-green color vision defects. Protan males can also either be

dichromatic, having only S cones and one type of M cone, or anomalous trichromatic, having S cones and two different M cone subtypes (**Table 1**).

Usually in protan and deutan defects, the cones are healthy and viable without significant loss of photoreceptors. For example, deuterans have only S cones and L cones, but the cells that would normally have become M cones usually are not lost, instead they become L cones. Likewise, protans usually are not missing the photoreceptors that would normally have become L cones, instead they become M cones. However, there are examples of protan and deutan defects in which cone photoreceptors are lost. Recently adaptive optics imaging was used to examine the retinas of several red-green color defective males, one of whom was estimated to have lost 30% of his cones. The individual was a dichromat (deuteranope), and cone-classing experiments using retinal densitometry plus adaptive optics showed that he had only S and L cones. His retina contained large dark (cone-less) areas, presumably where his M cones had been (26).

Although relatively rare, red-green color vision defects arise from mutations in either the *OPN1LW* or *OPN1MW* gene that result in an amino acid substitution (missense mutations) that inactivates the encoded opsin (26, 27). The most common such mutation is a substitution of arginine for cysteine at position 203 (C203R) of either the L or M opsin. Cysteine 203 participates in a highly conserved disulfide bond that is critical for proper folding of the cone opsin (28). Mutation of the corresponding cysteine in the rod pigment rhodopsin results in retinal degeneration (29). It is not known what happens to the cone photoreceptors expressing a C203R mutant photopigment, but this question will likely be addressed in the near future as high resolution adaptive optics imaging techniques become more available to examine affected patients.

Tritan defects are caused by missense mutations in the *OPN1SW* gene, and five such mutations have been reported to date (7-9, 30). Although the disorder is inherited, the color vision deficit is not always present from birth, instead it exhibits incomplete penetrance, meaning that not everyone who has a causative gene mutation has the color vision defect. A recent study using adaptive optics to image the retinas of a father and daughter, both with a tritan defect, revealed an absence of S cones in the father, but the presence of S cones in the daughter (9). These results suggest that some tritan defects may be associated with a progressive loss of S cones, and this would account for the

incomplete penetrance. That is, patients with the gene mutation may not exhibit a color vision deficiency until loss of S cones has progressed to a critical level at which the color defect manifests. The S-cone dystrophy hypothesized for tritan defects is analogous to rod dystrophy caused by rhodopsin mutations.

Inherited monochromatic color vision defects, termed achromatopsias, are associated with reduced (incomplete achromatopsia) or absent (complete achromatopsia) cone function. Blue cone monochromacy is an inherited form of incomplete achromatopsia characterized by the absence of functional L and M cones, with normal functional rods and S cones. Rod monochromacy is a form of complete achromatopsia characterized by the absence of all normal functioning cones (14, 31). Achromatopsias are bilateral defects accompanied by photophobia, nystagmus, and poor visual acuities, usually 20/200 or worse (5, 18, 32). The majority of cone photoreceptors in the human retina are L and M cones, with only about 5% being S cones (33, 34). Since cones serve high acuity vision the loss of function of ninety-five to one hundred percent of cones in achromatopsia accounts for the severe visual acuity deficits.

Acquired color vision defects: Losses in color vision can be acquired through systemic or ocular disease that affects the function of the visual system, or through exposure to neurotoxins. Acquired color vision defects are usually not present from birth, are often accompanied by other visual problems including decreased acuity and visual field defects, can affect one or both eyes, and usually become progressively worse (35-37). The mechanisms of pathology in chemical or disease induced color vision loss is not well understood.

ETIOLOGY

Inherited color vision defects: X-linked traits such as protan and deutan defects and blue cone monochromacy, are passed from mothers to sons. Females have two X-chromosomes and each X-chromosome has 50% chance of being passed to each of her offspring. Males have one X-chromosome, which they pass on to their daughters, and a Y-chromosome, which they pass on to their sons. If a female carries an X-linked color vision defect, her sons will have 50% chance of getting the X-chromosome with the defect, and thus of being affected by a color vision deficiency (Figure 2). A daughter of a

female carrier will also have 50% chance of receiving the X-chromosome with the defect. If a daughter receives the X-chromosome with the defect from her mother and a normal X-chromosome from her father, she will not be affected, because the normal X-chromosome will ensure that she will have both L and M cones. The daughter of a color defective father and a carrier mother may or may not be affected by a color vision defect (Figure 2). If her mother is a carrier of the same category of color vision defect, that affects her father, then she will have the same category of defect. However, if her mother carries a different category of red- green color vision defect compared to the defect her father has, the daughter will have normal color vision because, between her two X-chromosomes, the daughter will have genes that specify opsins for both L and M cones. If a female is a carrier of both blue cone monochromacy and a red-green color vision defect, she will be affected by the red-green color vision defect (Figure 2). The offspring of an affected male and a normal, non-carrier female will not have the color vision defect; however, all of the daughters will be carriers of the color vision defect, and thus will have 50% chance of passing it on to their sons.

Tritan color vision defects are autosomal dominant, and most affected people are heterozygous for the defect, having only one defective copy of the OPN1SW gene and one normal copy. In order to be homozygous for an OPN1SW mutation, the defect must be inherited both from the mother and from the father. Due to rarity of the defect, this generally only occurs when there is consanguinity in a family. Heterozygotes have 50% chance of passing the defect on to their offspring.

Rod monochromacies are autosomal recessive traits, a person will be affected only if they receive a gene defect both from their mother and from their father. Affected individuals have 50% chance of passing a defective gene on to their offspring.

Acquired color vision defects: People who suffer from diabetes, glaucoma, muscular dystrophy, multiple sclerosis, and optic neuropathies are all at risk for color vision loss as a secondary consequence of the disease. Occupational exposure to chemicals including solvents and metals is another risk factor for developing acquired color vision deficiency. Finally, a variety of drugs including those used to treat tuberculosis, epilepsy, and heart disease, can cause losses in color vision. Medications that have been reported to cause color vision loss are acetomenophen, ethanol,

chloroquine, digoxin, erythromycin, ethambutol, ibuprofen, indomethacin, nitroglycerin, oral contraceptives, quinine, salicylate, sildenafil citrate (Viagra), sulfonamides, thiazides, and tobacco (38)

PATHOPHYSIOLOGY

OPN1LW and OPN1MW each have six exons. The encoded pigments share 98% amino acid sequence identity, and whether a pigment is of the L-class versus M-class is determined by amino acids encoded by exon 5, which collectively produce a spectral difference of about 21 nm (Figure 3). L-class pigments have peak sensitivities near 560 nanometers (nm); M-class pigments have peak sensitivities near 530 nm (Figure 3). In L-class pigments, exons 2, 3, and 4 encode amino acid differences that produce spectral shifts of 2-3 nm, 3-4 nm, and 4 nm, respectively. In M-class pigments, exons 3 and 4 each encode amino acids that produce about a 3 nm spectral shift. Thus, L-class pigments have peak sensitivities spanning a range of about 10 nm, but M-class pigments have peak sensitivities spanning a range of only about 6 nm (**Figure 3**).

Protan and deutan color vision defects are most often caused by deletions and rearrangements that affect the OPN1LW and OPN1MW genes as illustrated in **Table 2**. OPN1LW and OPN1MW share greater than 98% nucleotide sequence identity over a span of about 40,000 base pairs of DNA (4, 39). As a consequence, during meiotic cell division in females, misalignment of two X-chromosomes allows unequal homologous recombination that produces new opsin gene arrays that differ in the number of opsin genes compared to the parental arrays and that contain chimeric genes that have segments from both parental OPN1LW and OPN1MW genes. The absorption spectra of the pigments encoded by the chimeric genes are determined by the complement of amino acids encoded at the spectral tuning sites (40-42).

As illustrated in Table 2 (top row), a cross-over between an L gene on one X-chromosome and an M gene on another X-chromosome produces an array in which the parental L and M genes are separated by a chimeric gene that encodes an L-class pigment. Despite the presence of a normal OPN1MW gene, a male inheriting this array will have a deutan color vision defect because the OPN1MW gene has been displaced to a non-expressed position. Only the first two genes in the array are usually expressed.

Males with a deutan color vision deficiency who have two different L-class pigments have color vision ranging from quite good (approaching normal) when the underlying pigments differ in peak sensitivity by about 10 nm, to dichromatic when the underlying pigments do not differ in peak sensitivity (23). Spectral separations intermediate between 0 and 10 nm give rise to the variation in phenotypes among deuteranomalous males (23, 24). The other product of the recombination is an array with a single gene that encodes an M-class pigment, thus a male inheriting this array will be a protanope (Table 2 top row).

The region downstream of the last gene in the X-chromosome opsin gene array is nearly identical to the region separating two adjacent opsin genes, and thus misaligned X-chromosomes can cross over in this region. As illustrated in **Table 2** (middle row), such a cross over produces two new arrays that differ in gene number compared to the parental arrays. The single gene array will confer dichromacy, protanopia in the illustrated case, on a male, while the three-gene array will confer normal color vision. In the human population, there is variation in the number of opsin genes on the X-chromosome, primarily in the number of OPN1MW genes. Crossovers that occur between arrays with different gene numbers are responsible for producing two new arrays, both of which confer a color vision defect in males, as illustrated in Table 2 (bottom panel). When an OPN1LW and an OPN1MW gene in arrays with different gene numbers undergo a recombination, one product is an array in which the first gene is a chimera and encodes an M class pigment, followed by an intact parental OPN1MW gene. Both genes encode M-class pigments, and the phenotype of a male inheriting such an array depends on the spectral separation between the two pigments, with better color vision being correlated with larger spectral separations. The other array contains two genes encoding L-class pigments and an OPN1MW gene in a non-expressed position, and thus produces a deutan defect, the severity of which is determined by the spectral separation between the L-class pigments.

Mixing of the OPN1LW and OPN1MW genes by recombination have produced combinations of the amino acids at the polymorphic positions that appear to be “poison combinations” that inactivate the photoreceptors that express them (43). For example, the deuteranope described above under Pathology for whom adaptive optics revealed large

patches of dark areas where cones should have been, had an intact OPN1MW gene that encoded an unusual combination of amino acids at the polymorphic positions encoded by exon 3. The same “poison combination” was also identified in blue cone monochromats as the cause of photoreceptor dysfunction (44).

Two genetic mechanisms have been identified as the cause of blue cone monochromacy. One mechanism is a combination of gene deletions and mutations that results in the absence of a gene on the X-chromosome that encodes a functional opsin (5, 6). The second mechanism is the deletion of a regulatory DNA element termed the locus control region (LCR) that lies upstream of the X-chromosome opsin genes and that plays a critical role in the expression of both OPN1LW and OPN1MW genes.

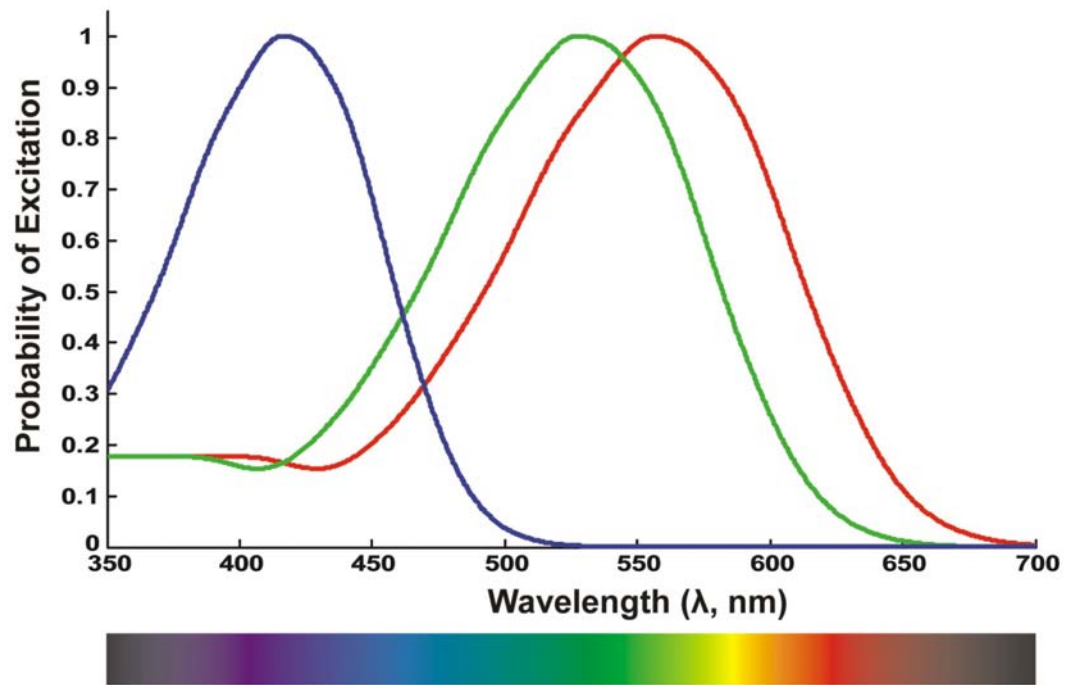
In rod monochromacy, there is evidence that cone photoreceptors are present and contain photopigments (5); however, the gene defects prevent the cones from signaling that light has been absorbed because they cannot effectively open and close ion channels in response to light.

Figure Captions

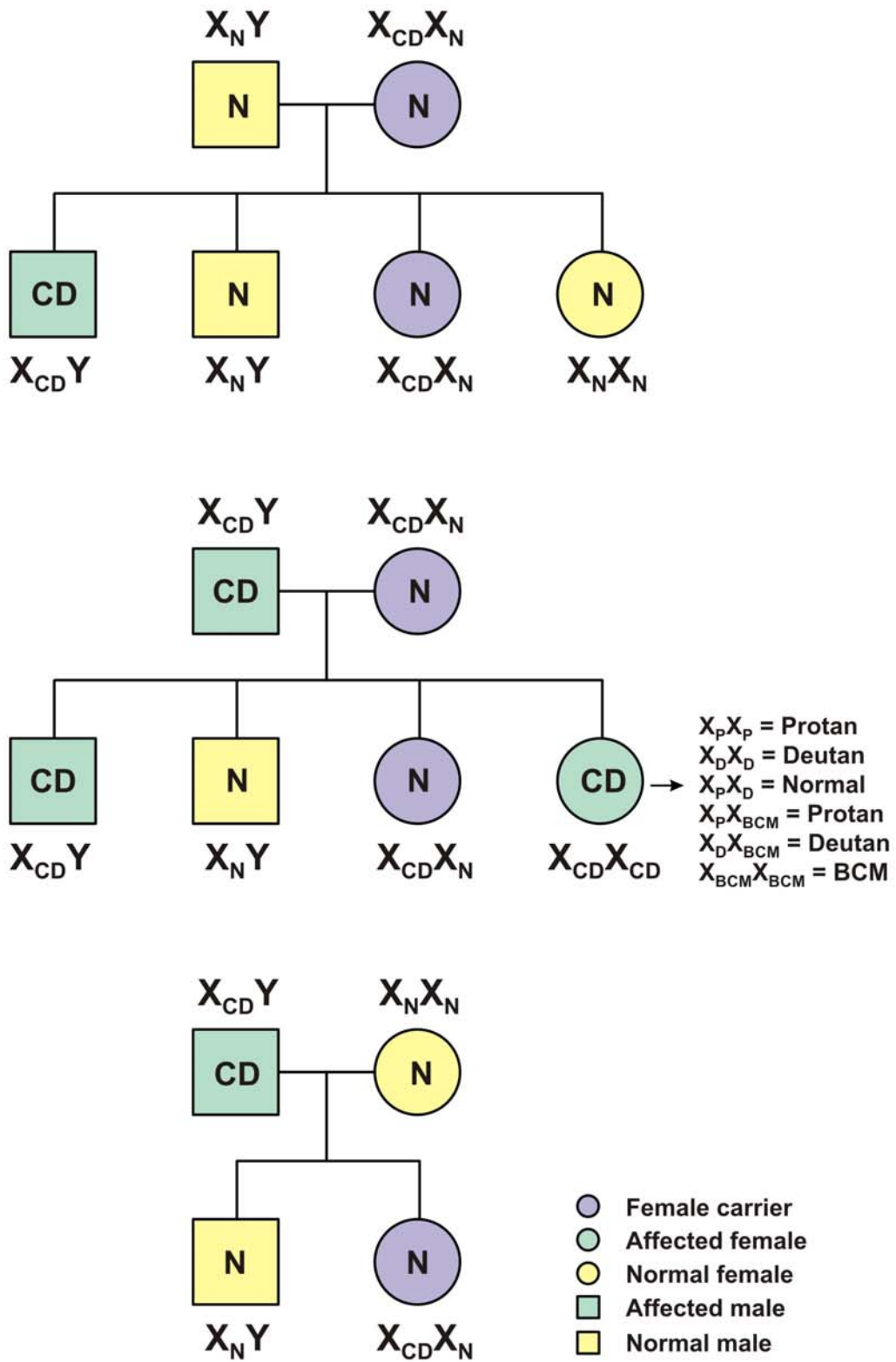
Figure 1. Relative spectral sensitivities of the three cone types that mediate normal human color vision expressed as a function of the probability (Y-axis) that an individual cone type will absorb light a specified wavelength (X-axis). The S cone has peak sensitivity at 415 nm, the M cone has peak sensitivity at ~530 nm, and the S cone has peak sensitivity ~560 nm. Below the graph of the spectral sensitivity functions is a representation of the color appearance of the wavelengths on the X-axis, as they would appear to a person with normal trichromatic color vision.

Figure 2. Inheritance of X-linked color vision deficiencies. X_{CD} – X-chromosome carrying a color vision defect, X_N – X-chromosome carrying normal color vision, X_{BCM} – X-chromosome carrying blue cone monochromacy. Squares indicate males, circles indicate females, the letters inside the squares and circles indicate the color vision phenotype of the individual with CD for color deficient and N for normal color vision. Top pedigree: possible offspring from a normal father and a mother that is a carrier of a color vision defect. Middle pedigree: possible offspring from an affected father and a carrier mother. Indicated to the right of the CD daughter are the possible color deficient phenotypes of a female with color deficiency on both X-chromosomes depending on the type of color defect carried by each of her X-chromosomes. Bottom pedigree: possible offspring from an affected father and a normal, non-carrier mother.

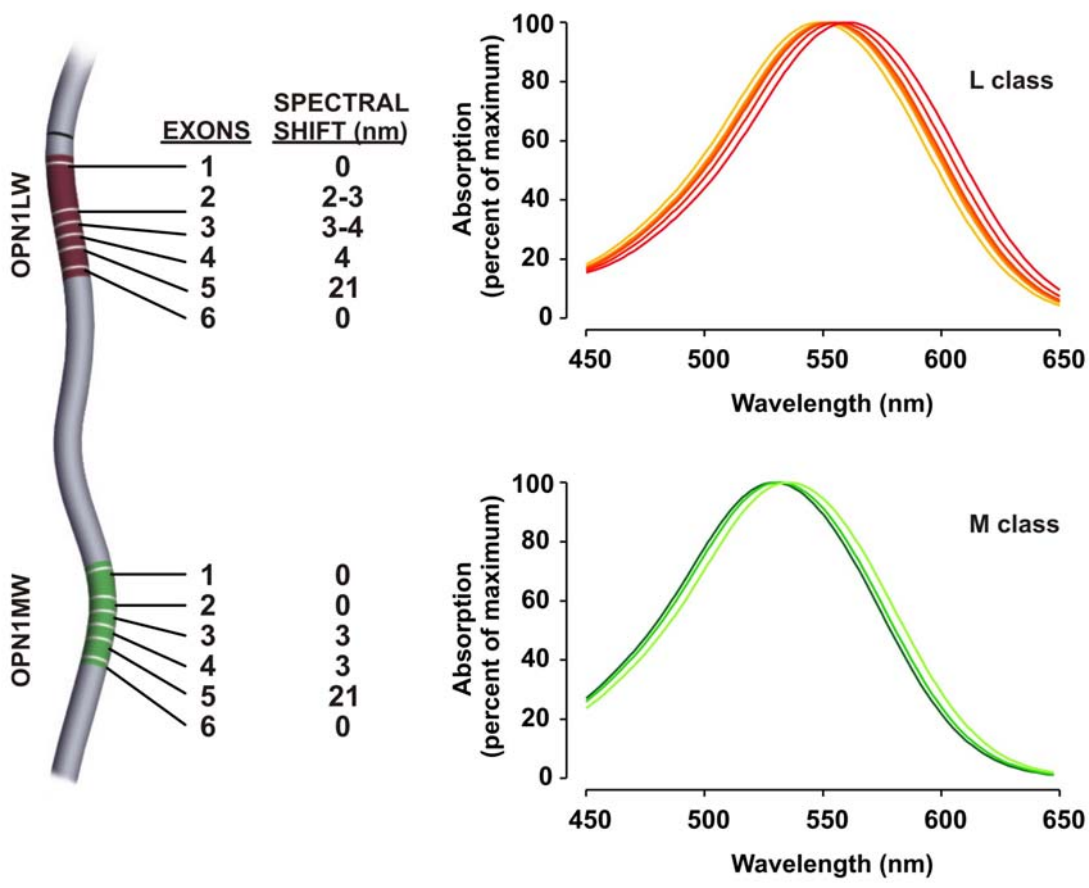
Figure 3. Genes and photopigments for red-green color vision. The structures of the OPN1LW and OPN1MW gene are drawn to scale with the exons (protein coding regions) indicated by number. The column labeled “spectral shift” gives the magnitude of the shift produced by polymorphic amino acid positions specified by individual exons. The absorption spectra of the L-class photopigments encoded by OPN1LW and the M-class photopigments specified by OPN1MW are shown to the right.



Neitz and Neitz, figure 1


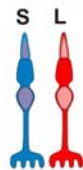
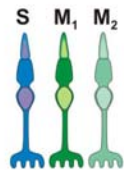



Neitz and Neitz, Figure 2



Neitz and Neitz, Figure 3

Table 1. Inherited Red-Green Color Vision Defects

Photoreceptors*	Percentage of red-green color vision defects	Term for the color vision phenotype	Term for affected person
<p>Deutan defects (6%)</p> 	5%	Deuteranomaly, anomalous trichromacy	Deuteranomalous, anomalous trichromat
	1%	Deuteranopia, dichromacy	Deuteranope, dichromat
<p>Protan defects (2%)</p> 	1%	Protanomaly, anomalous trichromacy	Protanomalous, anomalous trichromat
	1%	Protanopia, dichromacy	Protanope, dichromat

*L1 and L2 cones differ in spectral sensitivity, as do M1 and M2 cones.

Neitz and Neitz, Table 1

Table 2. Genetic mechanism for the common color vision defects.

Crossover	Recombination Product	Color Vision Phenotype
		Deutan (deuteranope or deuteranomalous) Protanope
		Normal Deuteranope
		Protan (protanope or protanomalous) Deutan (deuteranope or deuteranomalous)

L = L opsin, M = M opsin, NE = not expressed

Neitz and Neitz, Table 2

GLOSSARY AND QUICK REFERENCE FOR TERMS

Glossary of General Terms

Visual pigment (synonym: *photopigment*, *pigment*) are the light absorbing molecules in photoreceptors. They are composed of two parts – a protein component termed *opsin*, and a *chromophore*. In mammalian visual pigments, the chromophore is the vitamin A-derivative, *11-cis retinal*.

Missense mutation – a change in the protein coding sequence of a gene that results in a change in the amino acid sequence of the encoded protein.

Quick Reference for Terminology for Inherited color vision defects:

Protan – from the Greek for “the first,” defective color vision mediated by S cones and M cones with no L cone function. A category of red-green color vision deficiency.

Deutan – from the Greek for “the second,” color vision mediated by S cones and L cones with no M cone function. A category of red-green color vision deficiency.

Tritan – from the Greek for “the third,” color vision mediated by L and M cones with abnormal or no S cone function. Blue-yellow color vision deficiency.

Achromatopsia – vision mediated either by S cones and rods (*blue cone monochromacy*) or rods only (*rod monochromacy*)

Glossary of Official Gene Designations:

OPN1LW – X-chromosome gene encoding the opsin for the L cone photopigment.

OPN1MW- X-chromosome gene encoding the opsin for the M cone photopigment.

OPN1SW—chromosome 7 gene encoding the opsin for the S cone photopigment.

CNGA3—gene encoding the alpha subunit of the cyclic nucleotide gated ion channel that photoreceptors use to modulate membrane potential in response to light.

CNGB3 —gene encoding the beta subunit of the cyclic nucleotide gated ion channel that photoreceptors use to modulate membrane potential in response to light.

GNAT2—gene encoding the alpha subunit of transducin, the G-protein to which the cone photopigments, which are G-protein coupled receptors, are coupled.

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