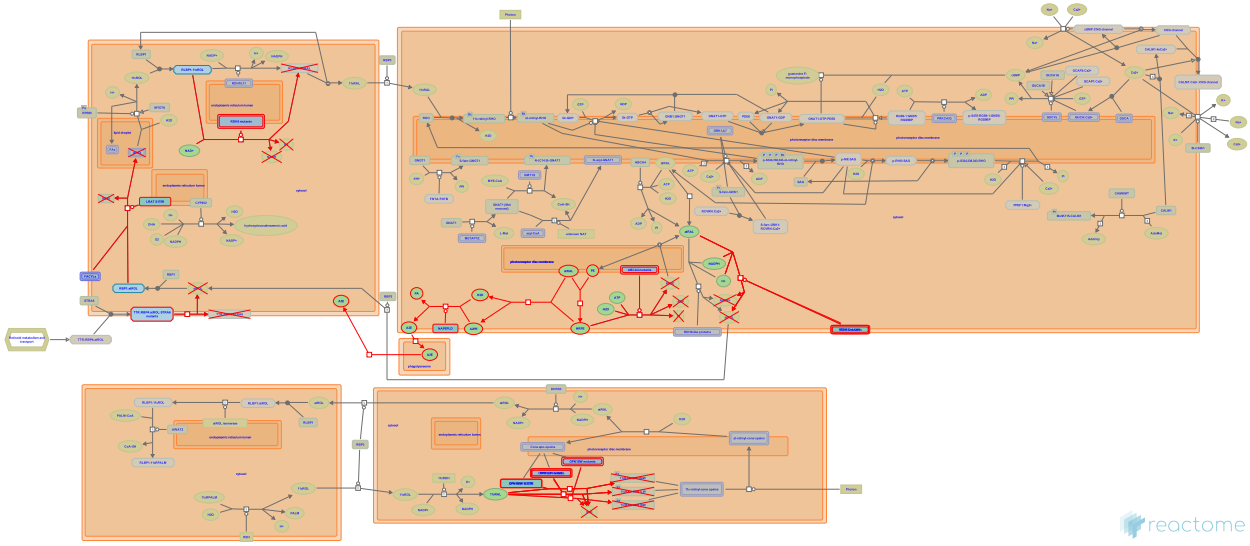
Retinoid cycle disease events



Blaner, WS., Jassal, B.

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28/09/2019

Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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Literature references

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Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

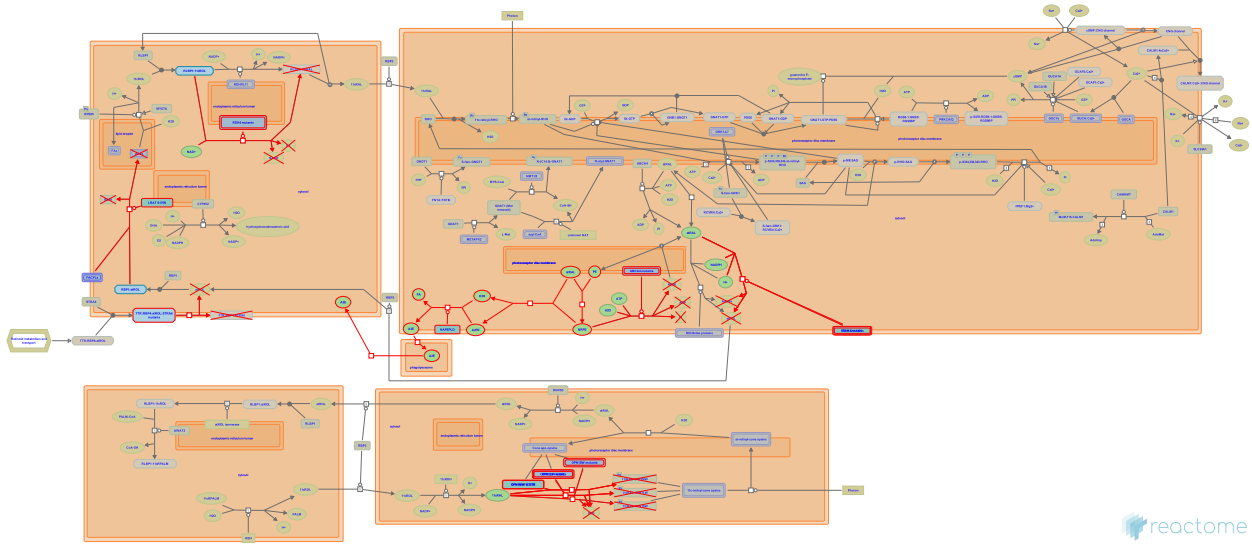
Reactome database release: 70

This document contains 2 pathways and 11 reactions (see Table of Contents)

Retinoid cycle disease events ↗

Stable identifier: R-HSA-2453864

Diseases: retinal disease



The gene defects which cause diseases related to the retinoid cycle are described here (Travis et al. 2007, Palczewski 2010, Fletcher et al. 2011, den Hollander et al. 2008).

Literature references

Travis, GH., Golczak, M., Moise, AR., Palczewski, K. (2007). Diseases caused by defects in the visual cycle: retinoids as potential therapeutic agents. *Annu. Rev. Pharmacol. Toxicol., 47*, 469-512. ↗

Fletcher, EL., Jobling, AI., Vessey, KA., Luu, C., Guymer, RH., Baird, PN. (2011). Animal models of retinal disease. *Prog Mol Biol Transl Sci, 100*, 211-86. ↗

den Hollander, AI., Roepman, R., Koenekoop, RK., Cremers, FP. (2008). Leber congenital amaurosis: genes, proteins and disease mechanisms. *Prog Retin Eye Res, 27*, 391-419. ↗

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Editions

2012-08-17	Authored, Edited	Jassal, B.
2013-01-31	Reviewed	Blaner, WS.

Defective STRA6 does not transport atROL ↗

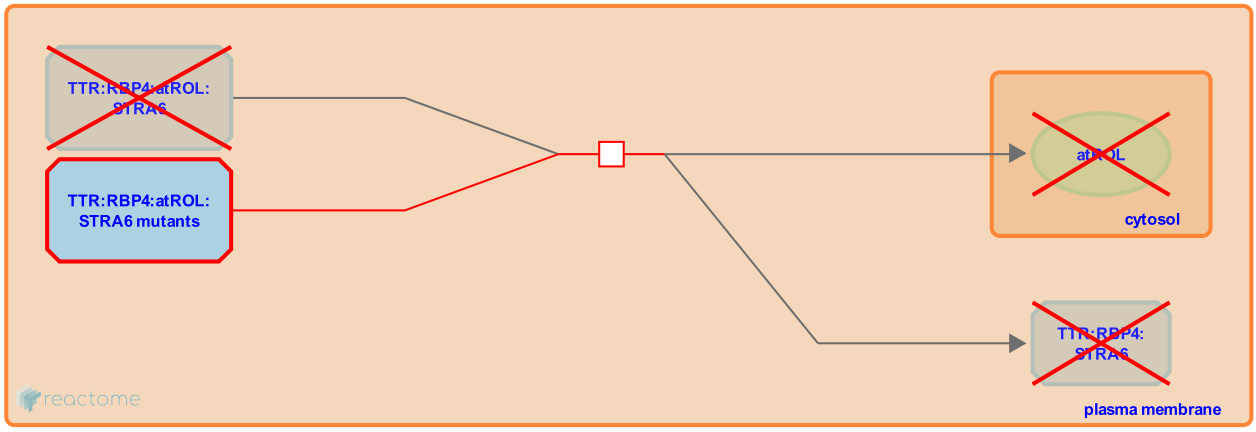
Location: Retinoid cycle disease events

Stable identifier: R-HSA-2453818

Type: transition

Compartments: plasma membrane

Diseases: microphthalmia



Defects in STRA6 cause microphthalmia syndromic type 9 (MCOPS9, Matthew-Wood syndrome or Spear syndrome; MIM:601186) (Chassaing et al. 2009). Mutiple systems are affected by this fatal syndrome including occular and cardiac abnormalities. Microphthalmia (also called microphthalmos, nanophthalmia or nanophthalmos) is a developmental disorder of the eye that literally means small eye and in most cases results in blindness. Common loss-of-function mutations causing MCOPS9 are P90L, P293L, and T321P, T644M, R655C (Pasutto et al. 2007) and W23* (West at al. 2009).

Literature references

Chassaing, N., Golzio, C., Odent, S., Lequeux, L., Vigouroux, A., Martinovic-Bouriel, J. et al. (2009). Phenotypic spectrum of STRA6 mutations: from Matthew-Wood syndrome to non-lethal anophthalmia. *Hum. Mutat., 30*, E673-81. ↗

Pasutto, F., Sticht, H., Hammersen, G., Gillessen-Kaesbach, G., FitzPatrick, DR., Nürnberg, G. et al. (2007). Mutations in STRA6 cause a broad spectrum of malformations including anophthalmia, congenital heart defects, diaphragmatic hernia, alveolar capillary dysplasia, lung hypoplasia, and mental retardation. *Am. J. Hum. Genet., 80*, 550-60. ↗

West, B., Bove, KE., Slavotinek, AM. (2009). Two novel STRA6 mutations in a patient with anophthalmia and diaphragmatic eventration. *Am. J. Med. Genet. A, 149*, 539-42. ↗

Editions

2012-08-17	Authored, Edited	Jassal, B.
2013-01-31	Reviewed	Blaner, WS.

Defective LRAT does not esterify RBP1:atROL and FACYLs to atREs ↗

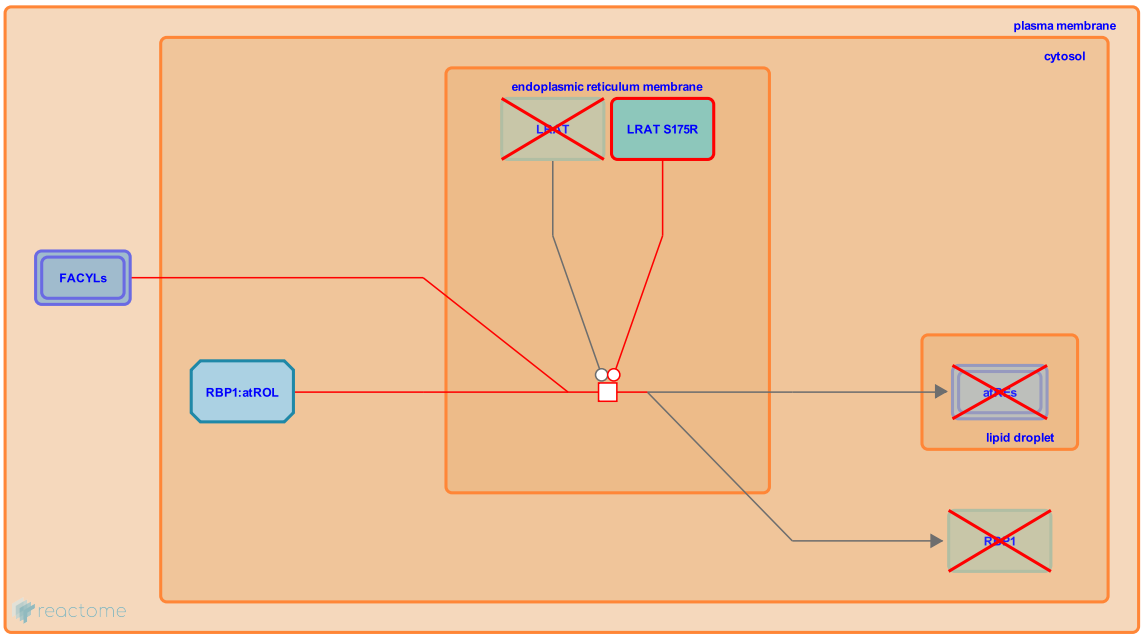
Location: Retinoid cycle disease events

Stable identifier: R-HSA-2466710

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol

Diseases: Leber congenital amaurosis



Normally functioning lecithin retinol acyltransferase (LRAT) mediates the transfer of an acyl group onto all-trans-retinol (atROL), forming retinyl esters (REs), the storage form of retinoids. Defects in LRAT cause Leber congenital amaurosis type 14 (LCA14, MIM:613341), an autosomal recessive juvenile-onset retinal dystrophy affecting rod and cone photoreceptors. Leber congenital amaurosis (LCA) comprises a group of early-onset retinal dystrophies characterized by vision loss, nystagmus, and severe retinal dysfunction (Chung & Traboulsi 2009). Loss of function is caused by the mutants S175R, 396delAA (Thompson et al. 2001) and 217delAT (Senechal et al. 2006, den Hollander et al. 2007) (the latter two not displayed).

Literature references

Chung, DC., Traboulsi, EI. (2009). Leber congenital amaurosis: clinical correlations with genotypes, gene therapy trials update, and future directions. *J AAPOS, 13*, 587-92. ↗

Thompson, DA., Li, Y., McHenry, CL., Carlson, TJ., Ding, X., Sieving, PA. et al. (2001). Mutations in the gene encoding lecithin retinol acyltransferase are associated with early-onset severe retinal dystrophy. *Nat. Genet., 28*, 123-4. ↗

Sénéchal, A., Humbert, G., Surget, MO., Bazalgette, C., Bazalgette, C., Arnaud, B. et al. (2006). Screening genes of the retinoid metabolism: novel LRAT mutation in leber congenital amaurosis. *Am. J. Ophthalmol., 142*, 702-4. ↗

den Hollander, AI., Lopez, I., Yzer, S., Zonneveld, MN., Janssen, IM., Strom, TM. et al. (2007). Identification of novel mutations in patients with Leber congenital amaurosis and juvenile RP by genome-wide homozygosity mapping with SNP microarrays. *Invest. Ophthalmol. Vis. Sci., 48*, 5690-8. ↗

Editions

2012-09-12	Authored, Edited	Jassal, B.
2013-01-31	Reviewed	Blaner, WS.

Defective ABCA4 does not transport NRPE from disc membranes ↗

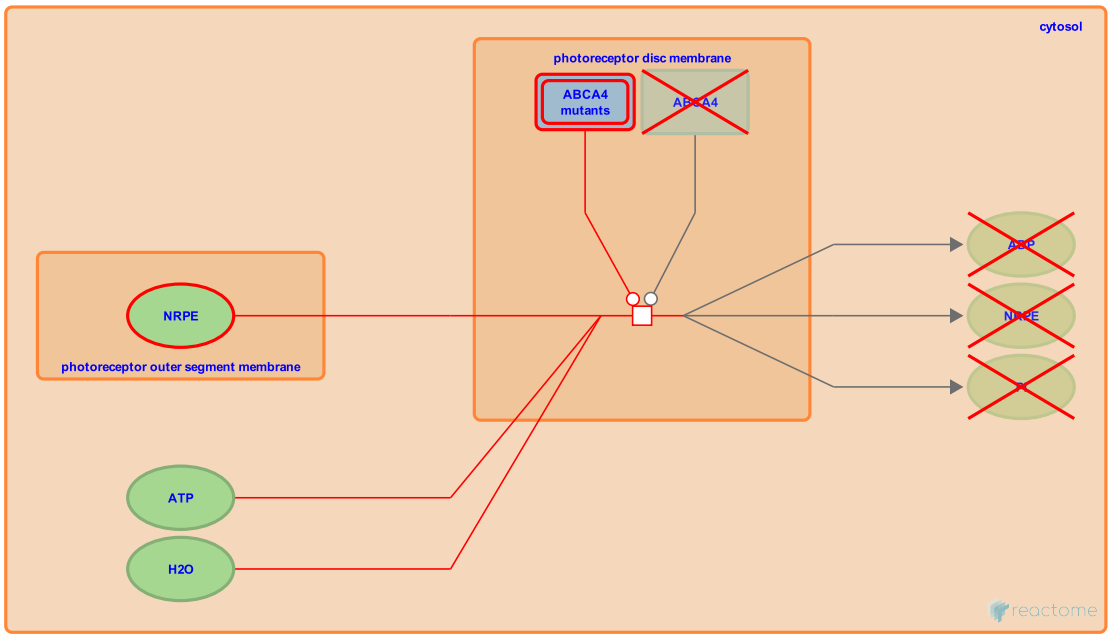
Location: Retinoid cycle disease events

Stable identifier: R-HSA-2466802

Type: transition

Compartments: photoreceptor disc membrane, cytosol, photoreceptor outer segment membrane

Diseases: macular degeneration



ATP-binding cassette protein A4 (ABCA4, ABCR), expressed exclusively in retinal photoreceptors, is thought to be involved in the clearance of toxic by-products of the retinoid cycle. Defects in ABCA4 cause a diverse range of human diseases. One such disease is Stargardt's disease type 1 (STGD1, MIM:248200) (Allikmets et al. 1997), an autosomal recessive form of juvenile macular degeneration leading to progressive irreversible loss of central vision and delayed dark adaptation. STGD1 was first identified by Stargardt in 1909 (Stargardt, Arch. Klin. Exp. Ophthal. 71: 534-549, 1909), has an approximate prevalence of 1 in 10,000 (see reviews Paskowitz et al. 2006, Walia & Fishman 2009) and is usually diagnosed within the first two decades of life.

The cause of retinal cell death is believed to be due to the accumulation of an age-related pigment called lipofuscin, which contains toxic by-products of the visual cycle (see review Sparrow et al. 2009). One prevelant toxic by-product, diretinoid-pyridinium-ethanolamine (A2E), is formed from condensation of two molecules of all-trans-retinal and one molecule of phosphatidylethanolamine (PE). Its precursors (atRAL and N-retinyl-phosphatidylethanolamine (NRPE)) are found in ocular tissues from Stargardt patients (Rozet et al. 1998). Another toxic intermediate is atRAL itself, the precursor to A2E. Studies in Abca4- and Rdh-deficient mice reveal atRAL's involvement in acute light-induced retinopathy (Maeda et al. 2009a, b).

Common mutations leading to STGD1 are A1038V, G1961E (Lewis et al. 1999), G863A (or delG863, not described here; Maugeri et al. 1999), R943Q (Allikmets et al. 1997) and T1428M (thought to be prevelant in 8% of the Japanese population; Kuroiwa et al. 1999).

Literature references

Rozet, JM., Gerber, S., Souied, E., Perrault, I., Châtelin, S., Ghazi, I. et al. (1998). Spectrum of ABCR gene mutations in autosomal recessive macular dystrophies. *Eur. J. Hum. Genet., 6*, 291-5. ↗

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Maeda, A., Maeda, T., Golczak, M., Chou, S., Desai, A., Hoppel, CL. et al. (2009). Involvement of all-trans-retinal in acute light-induced retinopathy of mice. *J. Biol. Chem., 284*, 15173-83. ↗

Allikmets, R., Singh, N., Sun, H., Shroyer, NF., Hutchinson, A., Chidambaram, A. et al. (1997). A photoreceptor cell-specific ATP-binding transporter gene (ABCR) is mutated in recessive Stargardt macular dystrophy. *Nat. Genet., 15*, 236-46. ↗

Editions

2012-09-12	Authored, Edited	Jassal, B.
2013-01-31	Reviewed	Blaner, WS.

Defective OPN1SW causes tritanopia ↗

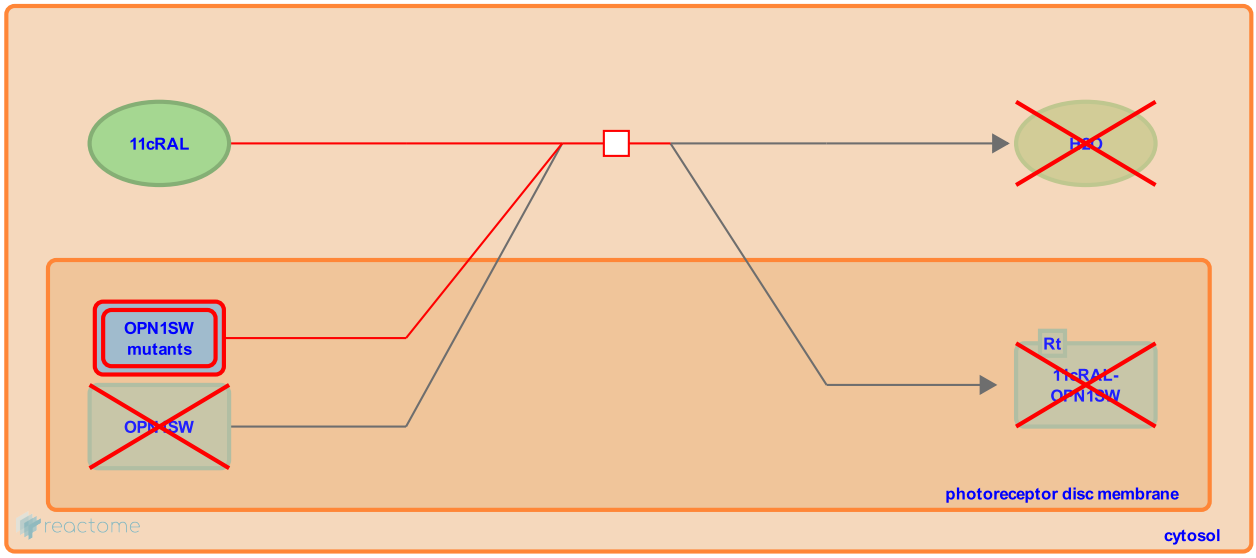
Location: Retinoid cycle disease events

Stable identifier: R-HSA-2466834

Type: transition

Compartments: cytosol, photoreceptor outer segment membrane

Diseases: blue color blindness



Normal human colour vision is trichromatic, based on 3 types of cones that are maximally sensitive to light at approximately 420 nm (blue cones), 530 nm (green cones), and 560 nm (red cones). Neural circuits compare light absorbed by these 3 cone types to perceive those primary colours and combinations of them. Colour vision deficiencies result from genetic mutations that affect the expression of the full complement of cone photoreceptors and are classified by severity of deficiency.

Anomolous trichromacy is the mildest form. Although affected individuals express all three cones, the way the cones process the primary colours is aberrant so discriminating various colours is difficult. Anomolous trichromacy is subdivided into protanomaly (affects red cones), deuteranomaly (affects green cones) and tritanomaly (affects blue cones). Dichromacy is the next severest colour vision deficiency. Dichromats have reduced colour vision based on the use of only 2 types of cone photoreceptors. Dichromacy is subdivided into protanopia (no functional red cones), deuteranopia (no functional green cones) and tritanopia (no functional blue cones). Monochromacy is the severest form of colour vision deficiency in which colour discrimination is absent due to dysfunctional or non-functional cones. All vision is therefore mediated by rods which otherwise usually function only in night conditions (see reviews Deeb 2005, Simunovic 2010).

Tritan (blue-yellow, blue colourblindness, tritanopia; MIM:190900) deficiencies are rare (1 in 500) (Went & Pronk 1985) compared to those involving green- and red-cone deficiencies. The first report of tritan defects was in 1952 (Wright 1952). Tritan deficiencies are inherited as autosomal dominant traits (Kalmus 1955) and are a result of missense mutations in the blue-cone photopigment gene OPN1SW, leading to amino-acid substitutions in the protein sequence. Tritan defects are characterized by a selective deficiency of blue spectral sensitivity (Weitz et al. 1992). Three amino-acid substitutions which cause deficiency or loss (or both) of blue-sensitive cone photoreceptors are Gly79Arg, Ser214Pro (Weitz et al. 1992) and Pro264Ser (Weitz et al. 1992b).

Literature references

Went, LN., Pronk, N. (1985). The genetics of tritan disturbances. *Hum. Genet., 69*, 255-62. ↗

KALMUS, H. (1955). The familial distribution of congenital tritanopia, with some remarks on some similar conditions. *Ann. Hum. Genet., 20*, 39-56. ↗

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Editions

2012-09-12	Authored, Edited	Jassal, B.
2013-01-31	Reviewed	Blaner, WS.

Defective OPN1MW causes DCB and BCM ↗

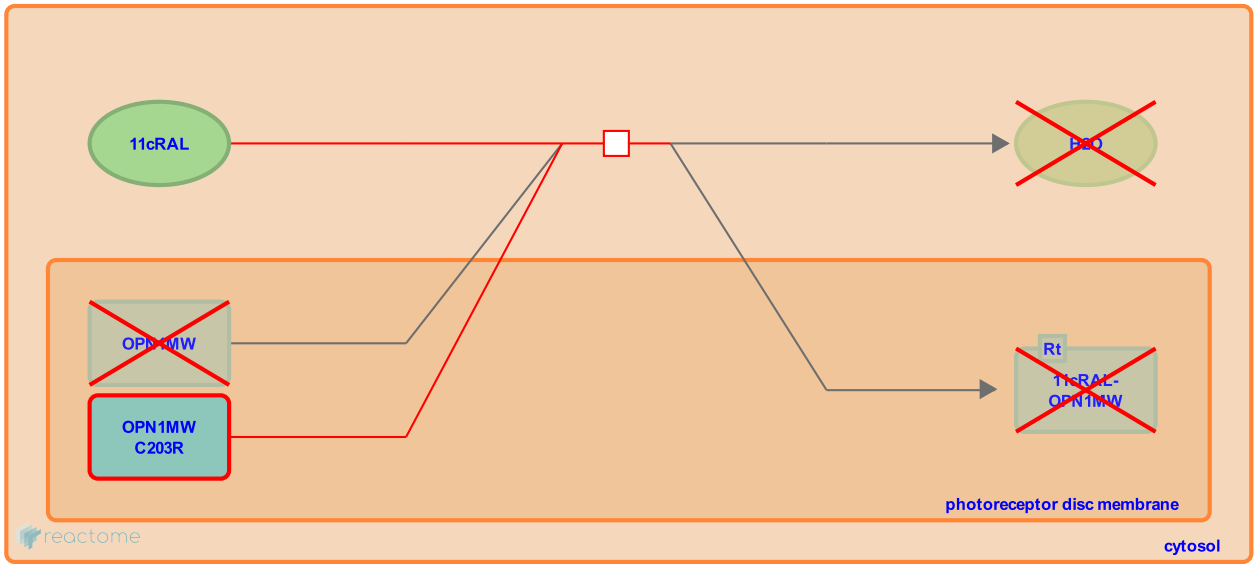
Location: Retinoid cycle disease events

Stable identifier: R-HSA-2466706

Type: transition

Compartments: cytosol, photoreceptor outer segment membrane

Diseases: blue cone monochromacy, red-green color blindness



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Deutan colourblindness (DCB, deuteranopia, partial colorblindness, green colourblindness; MIM:303800) is caused by mutations in the OPN1MW gene which encodes green cones. In European populations, red-green colourblindness is prevelant in 8% of males and 0.5% of females. This frequency is lower in non-European populations (Deeb 2005). The mutations C203R (Winderickx et al. 1992, Jagla et al. 2002), N94K and R330Q (Ueyama et al. 2002) can lead to DCB.

Blue cone monochromatism (BCM) is a rare X-linked congenital cone dysfunction characterized by the absence of functional long wavelength-sensitive (red) and medium wavelength-sensitive (green) cones in the retina. Colour discrimination is severely impaired from birth, and vision is derived from the pre-

served short wavelength-sensitive (blue) cones and rod photoreceptors. BCM typically presents with reduced visual acuity, pendular nystagmus, photophobia and patients often have myopia. BCM affects approximately 1 in 100,000 individuals (see review Gardner et al. 2009). The mutation C203R causes nonfunctional green and red cones (Nathans et al. 1989, Nathans et al. 1993, Reyniers et al. 1995).

Literature references

Jagla, WM., Jägle, H., Hayashi, T., Sharpe, LT., Deeb, SS. (2002). The molecular basis of dichromatic color vision in males with multiple red and green visual pigment genes. *Hum. Mol. Genet., 11*, 23-32.

Winderickx, J., Sanocki, E., Lindsey, DT., Teller, DY., Motulsky, AG., Deeb, SS. (1992). Defective colour vision associated with a missense mutation in the human green visual pigment gene. *Nat Genet, 1*, 251-6.

Ueyama, H., Kuwayama, S., Imai, H., Tanabe, S., Oda, S., Nishida, Y. et al. (2002). Novel missense mutations in red/green opsin genes in congenital color-vision deficiencies. *Biochem. Biophys. Res. Commun., 294*, 205-9.

Nathans, J., Davenport, CM., Maumenee, IH., Lewis, RA., Hejtmancik, JF., Litt, M. et al. (1989). Molecular genetics of human blue cone monochromacy. *Science, 245*, 831-8.

Nathans, J., Maumenee, IH., Zrenner, E., Sadowski, B., Sharpe, LT., Lewis, RA. et al. (1993). Genetic heterogeneity among blue-cone monochromats. *Am. J. Hum. Genet., 53*, 987-1000.

Editions

2012-09-12	Authored, Edited	Jassal, B.
2013-01-31	Reviewed	Blaner, WS.

Defective OPN1MW causes COD5 ↗

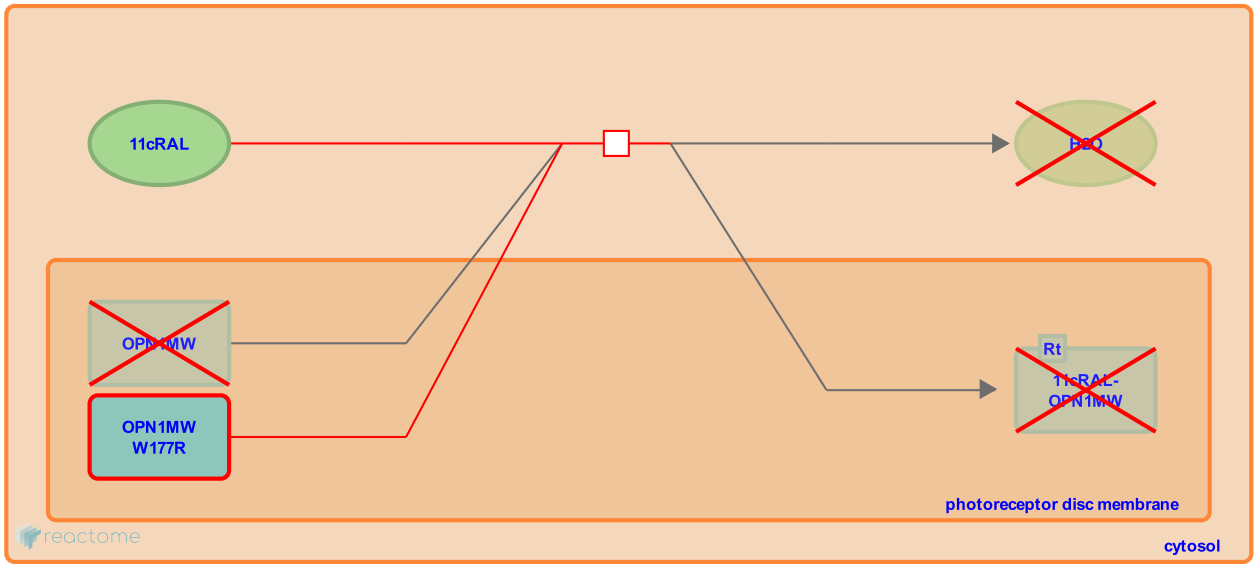
Location: Retinoid cycle disease events

Stable identifier: R-HSA-2471641

Type: transition

Compartments: cytosol, photoreceptor outer segment membrane

Diseases: cone-rod dystrophy



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Defects in OPN1MW cause X-linked cone dystrophy type 5 (COD5; MIM:303700), a retinal dystrophy characterized by progressive degeneration of cone photoreceptors but with preserved rod function. The W177R missense mutation in both the LW-sensitive (red) and MW-sensitive (green) cone opsin genes results in protein misfolding and retention in the endoplasmic reticulum which can lead to COD5 (Gardner et al. 2010).

Literature references

Gardner, JC., Webb, TR., Kanuga, N., Robson, AG., Holder, GE., Stockman, A. et al. (2010). X-linked cone dystrophy caused by mutation of the red and green cone opsins. *Am. J. Hum. Genet., 87*, 26-39. ↗

Editions

2012-09-21	Authored, Edited	Jassal, B.
2013-01-31	Reviewed	Blaner, WS.

Defective OPN1LW causes BCM ↗

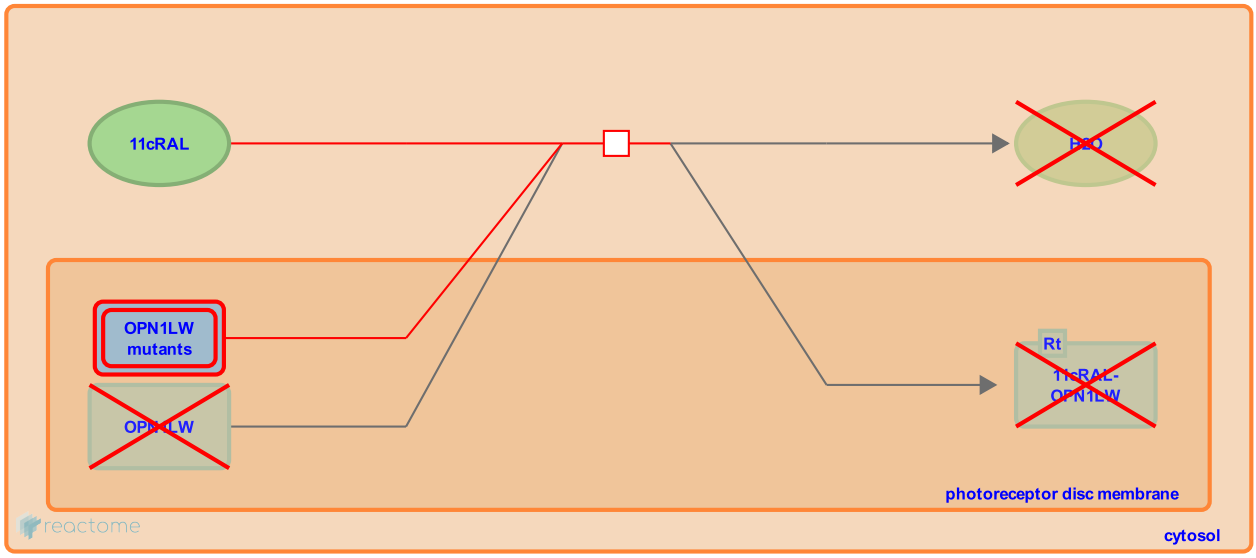
Location: Retinoid cycle disease events

Stable identifier: R-HSA-2466822

Type: transition

Compartments: cytosol, photoreceptor outer segment membrane

Diseases: blue cone monochromacy



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1989, Nathans et al. 1993, Reyniers et al. 1995).

Literature references

Reyniers, E., Van Thienen, MN., Meire, F., De Boulle, K., Devries, K., Kestelijn, P. et al. (1995). Gene conversion between red and defective green opsin gene in blue cone monochromacy. *Genomics, 29*, 323-8. ↗

Nathans, J., Maumenee, IH., Zrenner, E., Sadowski, B., Sharpe, LT., Lewis, RA. et al. (1993). Genetic heterogeneity among blue-cone monochromats. *Am. J. Hum. Genet., 53*, 987-1000. ↗

Nathans, J., Davenport, CM., Maumenee, IH., Lewis, RA., Hejtmancik, JF., Litt, M. et al. (1989). Molecular genetics of human blue cone monochromacy. *Science, 245*, 831-8. ↗

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Editions

2012-09-12	Authored, Edited	Jassal, B.
2013-01-31	Reviewed	Blaner, WS.

Defective OPN1LW causes CBP ↗

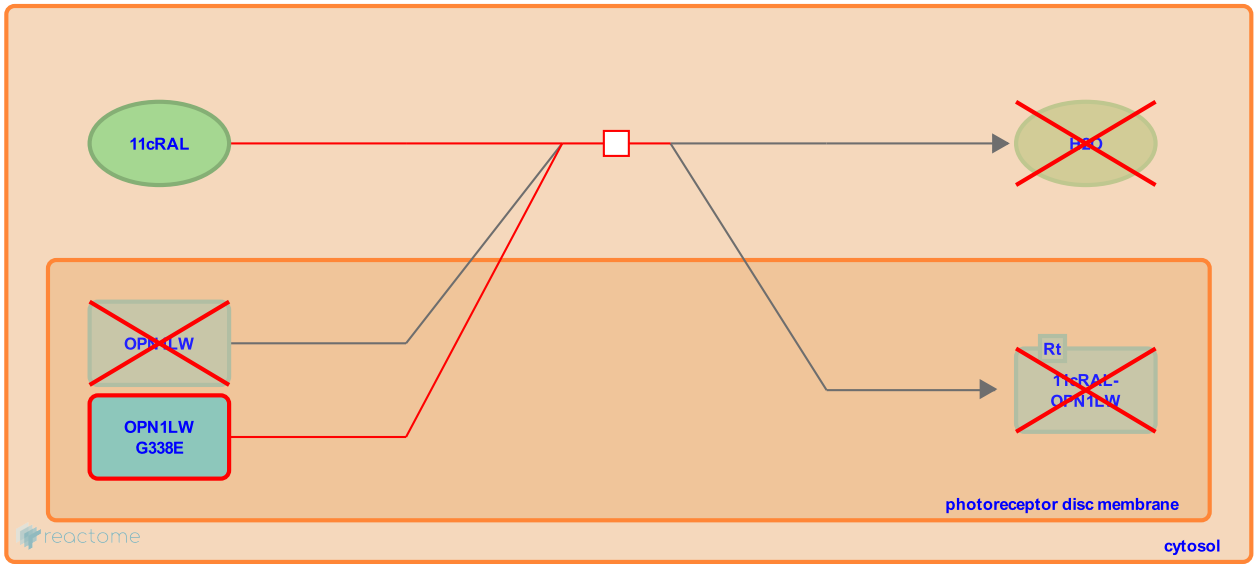
Location: Retinoid cycle disease events

Stable identifier: R-HSA-2471660

Type: transition

Compartments: cytosol, photoreceptor outer segment membrane

Diseases: red color blindness



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Defects in OPN1LW cause partial colorblindness, protan series (CBP, protanopia; MIM:303900) due to non-functional red cones. The mutation G338E causes CBP (Ueyama et al. 2002).

Literature references

Ueyama, H., Kuwayama, S., Imai, H., Tanabe, S., Oda, S., Nishida, Y. et al. (2002). Novel missense mutations in red/green opsin genes in congenital color-vision deficiencies. *Biochem. Biophys. Res. Commun., 294*, 205-9. ↗

Editions

2012-09-21	Authored, Edited	Jassal, B.
2013-01-31	Reviewed	Blaner, WS.

Defective RDH12 does not reduce atRAL to atROL and causes LCA13 ↗

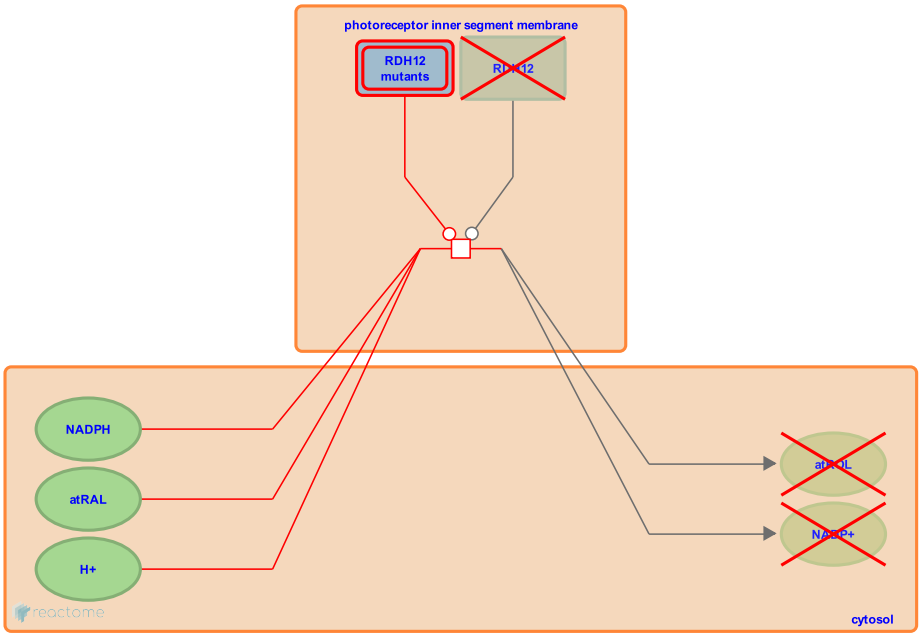
Location: Retinoid cycle disease events

Stable identifier: R-HSA-2466861

Type: transition

Compartments: photoreceptor inner segment membrane, cytosol

Diseases: Leber congenital amaurosis



Retinol dehydrogenase RDH12 mediates the reversible, NADP(H)-dependent reduction of all-trans-retinal (atRAL) or 11-cis-retinal (11cRAL) to all-trans-retinol (atROL) or 11-cis-retinol (11cROL) respectively in photoreceptor cells.

Defects in RDH12 cause Leber congenital amaurosis type 13 (LCA13; MIM:612712). LCA defects are early-onset and severe retinal degenerations that are responsible for the most common cause of congenital blindness in infants and children. Mutants that abolish RDH12 activity to result in LCA13 are Y226C, Q189X (Janecke et al, 2004), p.Ala269fxX270 (Perault et al. 2004, Janecke et al, 2004) and H151N (Perault et al. 2004).

Literature references

Janecke, AR., Thompson, DA., Utermann, G., Becker, C., Hübner, CA., Schmid, E. et al. (2004). Mutations in RDH12 encoding a photoreceptor cell retinol dehydrogenase cause childhood-onset severe retinal dystrophy. *Nat. Genet. , 36*, 850-4. ↗

Perrault, I., Hanein, S., Gerber, S., Barbet, F., Ducroq, D., Dollfus, H. et al. (2004). Retinal dehydrogenase 12 (RDH12) mutations in leber congenital amaurosis. *Am. J. Hum. Genet., 75*, 639-46. ↗

Editions

2012-09-12	Authored, Edited	Jassal, B.
2013-01-31	Reviewed	Blaner, WS.

Defective RDH12 does not reduce atRAL to atROL ↗

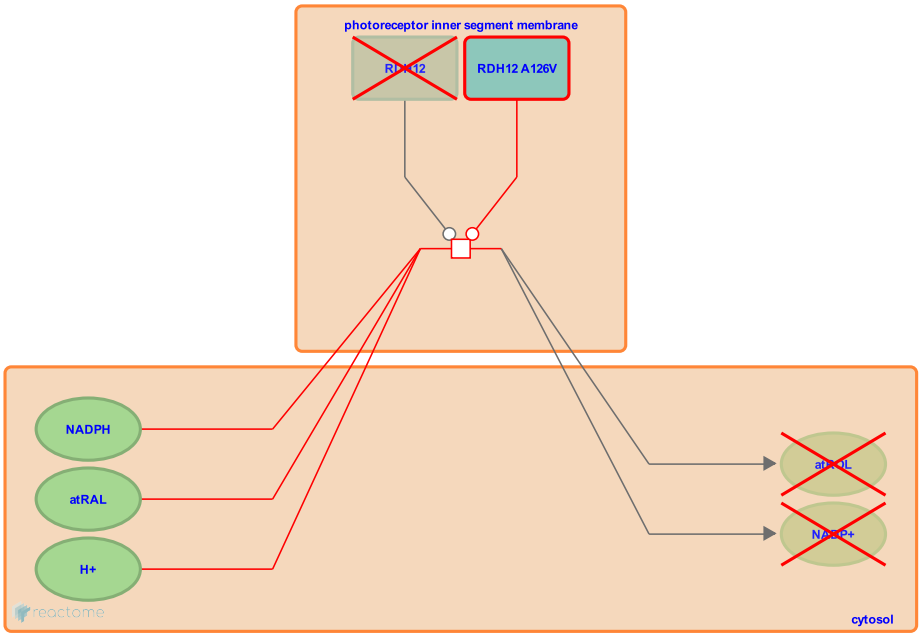
Location: Retinoid cycle disease events

Stable identifier: R-HSA-2471670

Type: transition

Compartments: photoreceptor inner segment membrane, cytosol

Diseases: retinitis pigmentosa



Retinol dehydrogenase RDH12 mediates the reversible, NADP(H)-dependent reduction of all-trans-retinal (atRAL) or 11-cis-retinal (11cRAL) to all-trans-retinol (atROL) or 11-cis-retinol (11cROL) respectively in photoreceptor cells.

Defects in RDH12 cause retinitis pigmentosa type 53 (RP53; MIM:612712), an autosomal recessive retinal dystrophy characterised by retinal pigment deposits and primary loss of rod photoreceptor cells followed by secondary loss of cone photoreceptor cells. The A126V mutant causes RP53 (Benayoun et al. 2009).

Literature references

Benayoun, L., Spiegel, R., Auslender, N., Abbasi, AH., Rizel, L., Hujeirat, Y. et al. (2009). Genetic heterogeneity in two consanguineous families segregating early onset retinal degeneration: the pitfalls of homozygosity mapping. *Am. J. Med. Genet. A, 149*, 650-6. ↗

Editions

2012-09-21	Authored, Edited	Jassal, B.
2013-01-31	Reviewed	Blaner, WS.

Defective RDH5 does not oxidise 11cROL to 11cRAL and causes RPA ↗

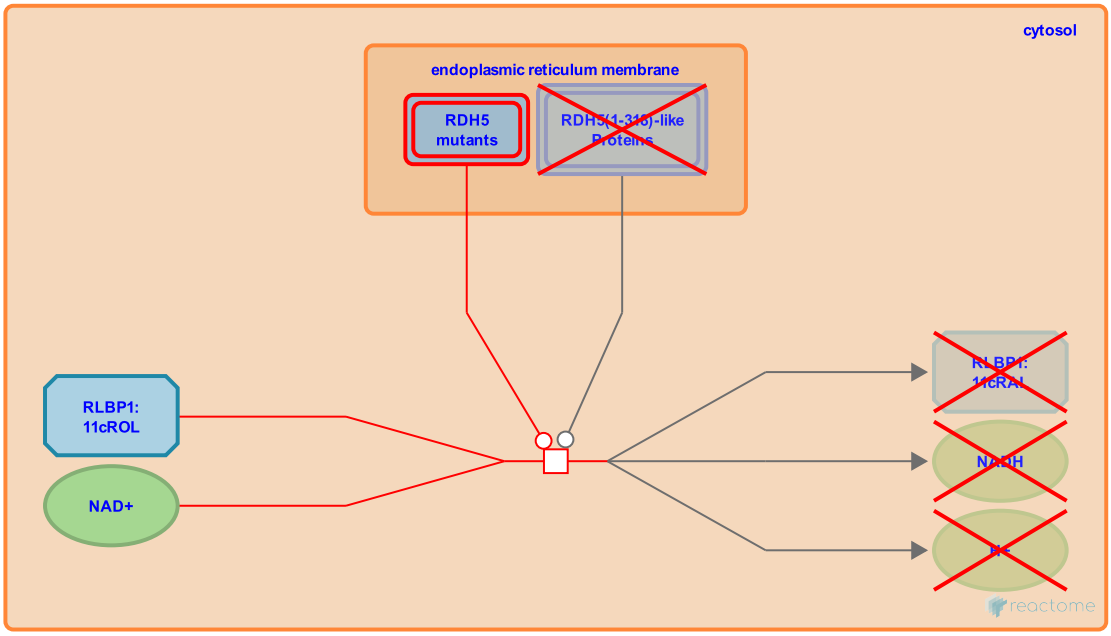
Location: Retinoid cycle disease events

Stable identifier: R-HSA-2466832

Type: transition

Compartments: cytosol, endoplasmic reticulum membrane

Diseases: fundus albipunctatus



11-cis-retinol dehydrogenase (RDH5) can reversibly catalyse the oxidation of all-trans-retinol (atROL, bound to RLBP1) to all-trans-retinal (atRAL) in retinal pigment epithelium (RPE) cells using NAD+ as cofactor. Defective RDH5 causes retinitis punctata albescens (RPA, also called fundus albipunctatus, FA; MIM:136880). RPA (an autosomal recessive disorder) is a form of stationary congenital night blindness characterised by a reduced regeneration rate of rod and cone photoreceptors and yellow-white lesions within the retina or the RPE. Mutations causing RPA include G238W (Gonzalez-Fernandez et al. 1999, Yamamoto et al. 1999), R280H (Gonzalez-Fernandez et al. 1999, Kuroiwa et al. 2000, Nakamura et al. 2000), A294P (Gonzalez-Fernandez et al. 1999), V177G (Gonzalez-Fernandez et al. 1999, Kuroiwa et al. 2000) and R157W (Cideciyan et al. 2000).

Literature references

Gonzalez-Fernandez, F., Kurz, D., Bao, Y., Newman, S., Conway, BP., Young, JE. et al. (1999). 11-cis retinol dehydrogenase mutations as a major cause of the congenital night-blindness disorder known as fundus albipunctatus. *Mol. Vis., 5*, 41. ↗

Yamamoto, H., Simon, A., Eriksson, U., Harris, E., Berson, EL., Dryja, TP. (1999). Mutations in the gene encoding 11-cis retinol dehydrogenase cause delayed dark adaptation and fundus albipunctatus. *Nat. Genet., 22*, 188-91. ↗

Kuroiwa, S., Kikuchi, T., Yoshimura, N. (2000). A novel compound heterozygous mutation in the RDH5 gene in a patient with fundus albipunctatus. *Am. J. Ophthalmol., 130*, 672-5. ↗

Cideciyan, AV., Haeseleer, F., Fariss, RN., Aleman, TS., Jang, GF., Verlinde, CL. et al. (2000). Rod and cone visual cycle consequences of a null mutation in the 11-cis-retinol dehydrogenase gene in man. *Vis. Neurosci., 17*, 667-78. ↗

Nakamura, M., Hotta, Y., Tanikawa, A., Terasaki, H., Miyake, Y. (2000). A high association with cone dystrophy in Fundus albipunctatus caused by mutations of the RDH5 gene. *Invest. Ophthalmol. Vis. Sci., 41*, 3925-32. ↗

Editions

2012-09-12	Authored, Edited	Jassal, B.
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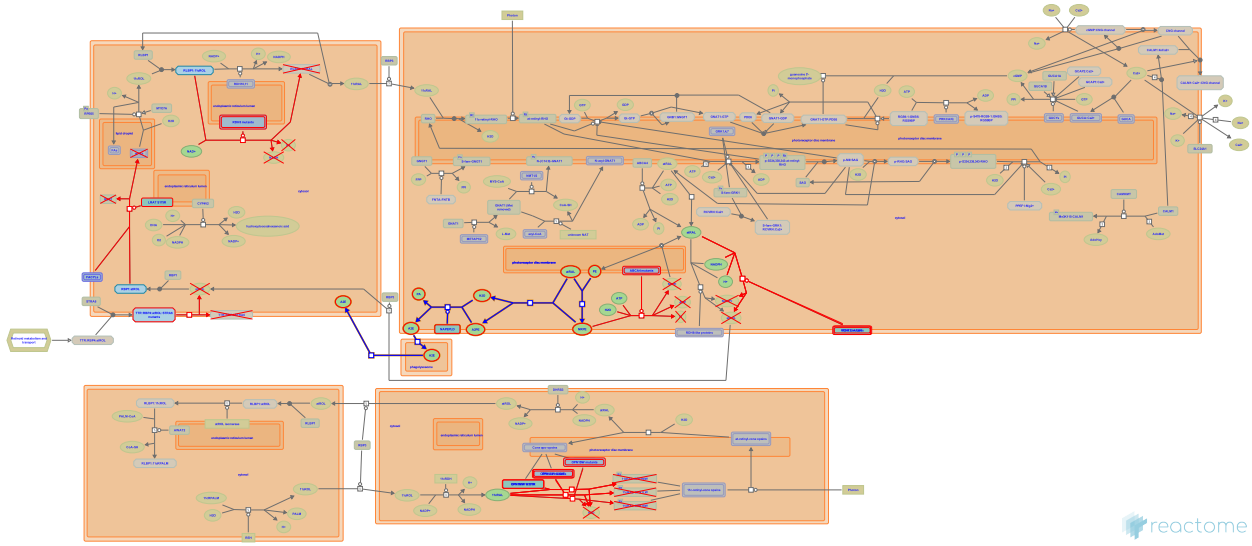
Biosynthesis of A2E, implicated in retinal degradation ↗

Location: Retinoid cycle disease events

Stable identifier: R-HSA-2466712

Diseases: dystrophies primarily involving the retinal pigment epithelium



Lipofuscin is a yellow-brown pigment grain composed mainly of lipids but also sugars and certain metals. Accumulation of lipofuscin is associated with degenerative diseases such as Alzheimer's disease, Parkinson's disease, chronic obstructive pulmonary disease and retinal macular degeneration.

A prominent component of lipofuscin in retinal pigment epithelial (RPE) cells is the bisretinoid A2E (di-retinoid-pyridinium-ethanolamine), the end-product of the condensation of 2 molecules of all-trans-retinal (atRAL) and phosphatidylethanolamine (PE) in photoreceptor outer disc membranes. Once formed, A2E is phagocytosed, together with outer segments (Kevany & Palczewski 2010), to RPE where it accumulates. There is no evidence as yet to indicate that A2E can be catabolised (Sparrow et al. 2012, Sparrow et al. 2010). A simplified biosynthetic pathway for A2E is described here.

Literature references

Sparrow, JR., Gregory-Roberts, E., Yamamoto, K., Blonska, A., Ghosh, SK., Ueda, K. et al. (2012). The bisretinoids of retinal pigment epithelium. *Prog Retin Eye Res, 31*, 121-35. ↗

Sparrow, JR., Wu, Y., Kim, CY., Zhou, J. (2010). Phospholipid meets all-trans-retinal: the making of RPE bisretinoids. *J. Lipid Res., 51*, 247-61. ↗

Kevany, BM., Palczewski, K. (2010). Phagocytosis of retinal rod and cone photoreceptors. *Physiology (Bethesda), 25*, 8-15. ↗

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2012-09-12	Authored, Edited	Jassal, B.
2013-01-31	Reviewed	Blaner, WS.

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