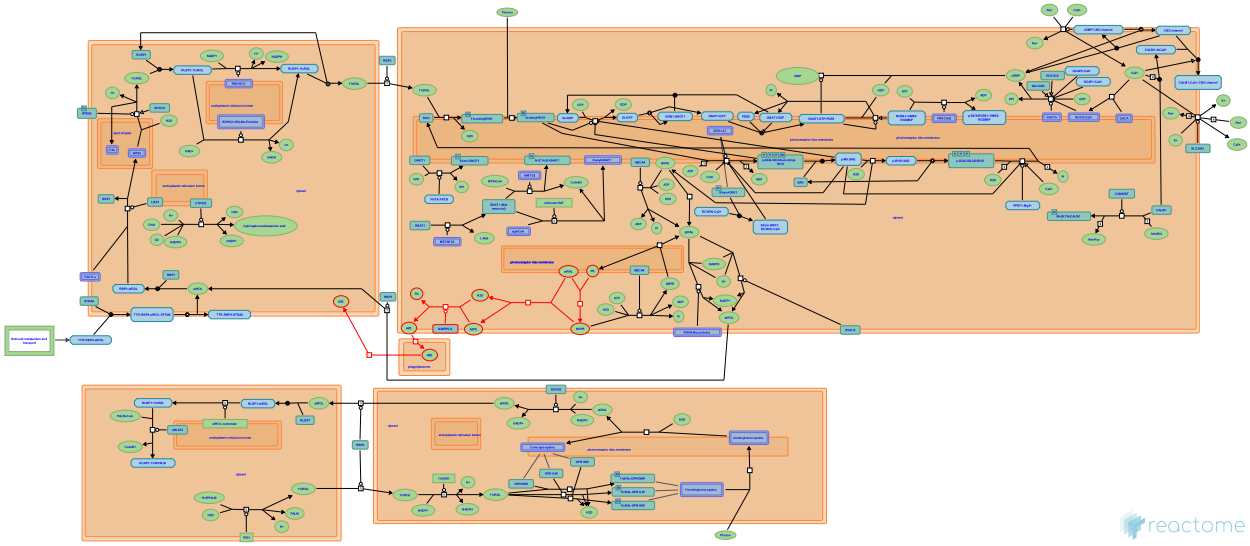
Visual phototransduction



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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.
The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

Literature references

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18*, 142. ↗

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

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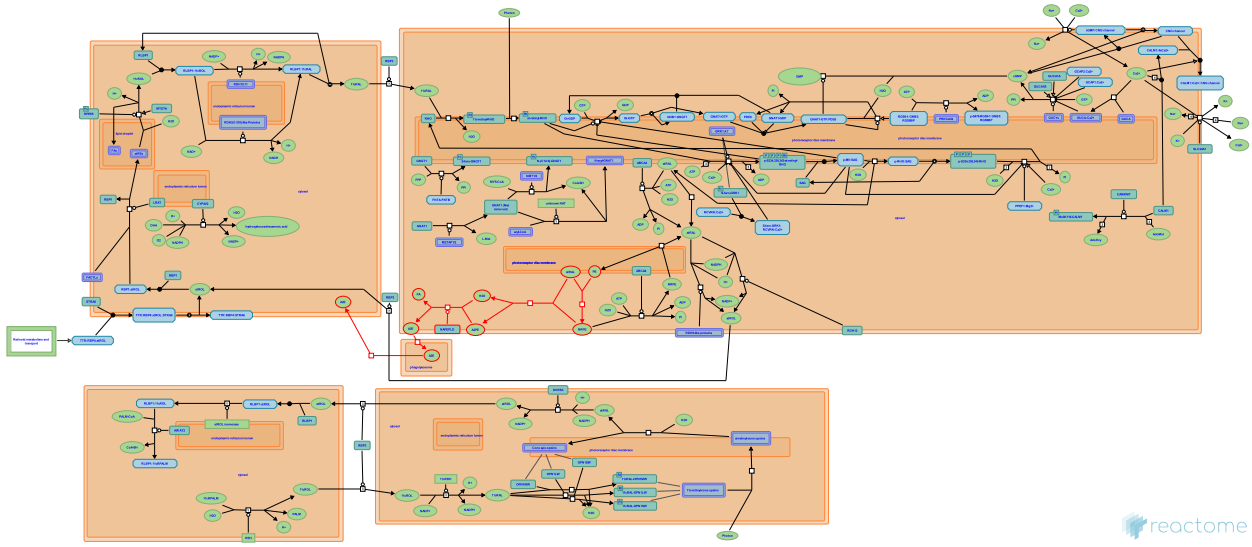
Reactome database release: 88

This document contains 5 pathways (see Table of Contents)

Visual phototransduction ↗

Stable identifier: R-HSA-2187338



Visual phototransduction is the process by which photon absorption by visual pigment molecules in photoreceptor cells is converted to an electrical cellular response. The events in this process are photochemical, biochemical and electrophysiological and are highly conserved across many species. This process occurs in two types of photoreceptors in the retina, rods and cones. Each type consists of two parts, the outer segment which detects a photon signal and the inner segment which contains the necessary machinery for cell metabolism. Each type of cell functions differently. Rods are very light sensitive but their flash response is slow so they work best in twilight conditions but are not good at detecting objects moving quickly. Cones are less light-sensitive and have a fast flash response so they work best in daylight conditions and are better at detecting fast moving objects than rods.

The visual pigment consists of a chromophore (11-cis-retinal, 11cRAL, A1) covalently attached to a GPCR opsin family member. The linkage is via a Schiff base forming retinylidene protein. Upon photon absorption, 11cRAL isomerises to all-trans retinal (atRAL), changing the conformation of opsin to an activated form which can activate the regulatory G protein transducin (Gt). The alpha subunit of Gt activates phosphodiesterase which hydrolyses cGMP to 5'-GMP. As high level of cGMP keep cGMP-gated sodium channels open, the lowering of cGMP levels closes these channels which causes hyperpolarization of the cell and subsequently, closure of voltage-gated calcium channels. As calcium levels drop, the level of the neurotransmitter glutamate also drops causing depolarization of the cell. This effectively relays the light signal to postsynaptic neurons as electrical signal (Burns & Pugh 2010, Korenbrot 2012, Pugh & Lamb 1993).

11cRAL cannot be synthesised in vertebrates. Vitamin A from many dietary sources is the precursor for 11cRAL. It is taken from food in the form of esters such as retinyl acetate or palmitate or one of four caretenoids (alpha-carotene, beta-carotene, gamma-carotene and beta-cryptoxanthin). Retinoids are transported from the gut to be stored in liver, until required by target organs such as the eye (Harrison & Hussain 2001, Harrison 2005). In the eye, in the form 11cRAL, it is used in the retinoid (visual) cycle to initiate phototransduction and for visual pigment regeneration to ready the photoreceptor for the next phototransduction event (von Lintig 2012, Blomhoff & Blomhoff 2006, von Lintig et al. 2010, D'Ambrosio et al. 2011, Wang & Kefalov 2011, Kefalov 2012, Wolf 2004).

Literature references

Pugh, EN., Lamb, TD. (1993). Amplification and kinetics of the activation steps in phototransduction. *Biochim. Biophys. Acta, 1141*, 111-49. ↗

Korenbrot, JI. (2012). Speed, sensitivity, and stability of the light response in rod and cone photoreceptors: facts and models. *Prog Retin Eye Res, 31*, 442-66. ↗

Kefalov, VJ. (2012). Rod and cone visual pigments and phototransduction through pharmacological, genetic, and physiological approaches. *J. Biol. Chem., 287*, 1635-41. ↗

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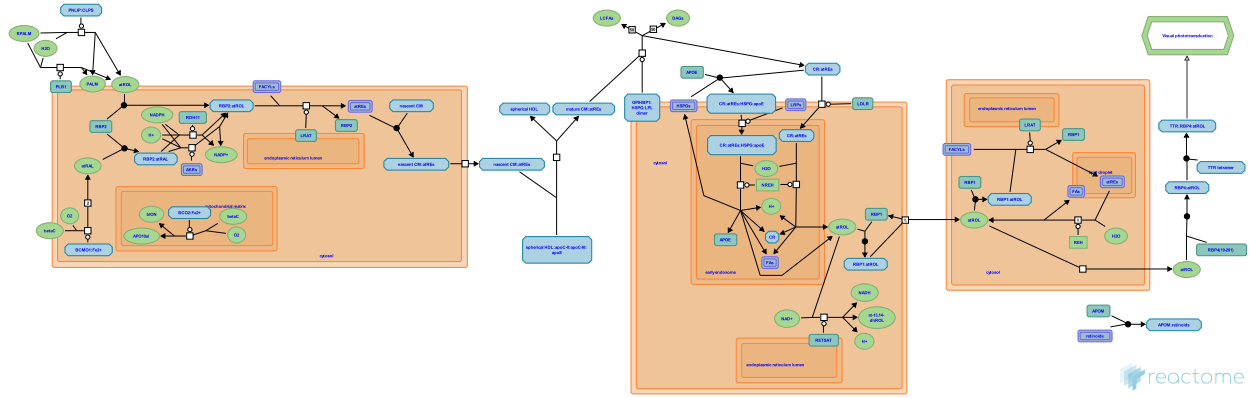
Editions

2012-04-09	Authored, Edited	Jassal, B.

Retinoid metabolism and transport ↗

Location: Visual phototransduction

Stable identifier: R-HSA-975634



Vitamin A (all-trans-retinol) must be taken up, either as carotenes from plants, or as retinyl esters from animal food. The most prominent carotenes are alpha-carotene, lycopene, lutein, beta-cryptoxanthine, and especially beta-carotene. After uptake they are mostly broken down to retinal. Retinyl esters are hydrolysed like other fats. In enterocytes, retinoids bind to retinol-binding protein (RBP). Transport from enterocytes to the liver happens via chylomicrons (Harrison & Hussain 2001, Harrison 2005).

Literature references

Harrison, EH. (2005). Mechanisms of digestion and absorption of dietary vitamin A. *Annu Rev Nutr, 25*, 87-103. ↗

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Editions

2010-09-19	Authored	Stephan, R.
2010-10-01	Authored, Edited	Jassal, B.
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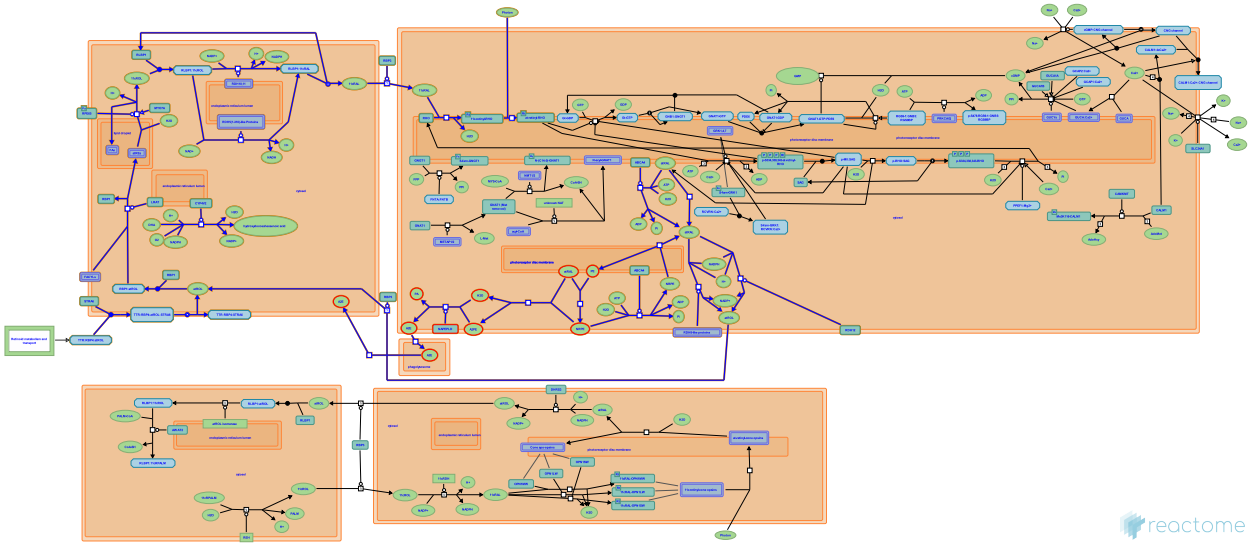
2013-01-31	Reviewed	Blaner, WS.
2013-01-31	Revised	Jassal, B.

The canonical retinoid cycle in rods (twilight vision)

Location: Visual phototransduction

Stable identifier: R-HSA-2453902



The retinoid cycle (also referred to as the visual cycle) is the process by which the visual chromophore 11-cis-retinal (11cRAL) is released from light-activated opsins in the form all-trans-retinal and isomerized back to its 11-cis isomer ready for another photoisomerization reaction. This process involves oxidation, reduction and isomerization reactions and take place in the retinal pigment epithelium (RPE) and photoreceptor segments of the eye (von Lintig 2012, Blomhoff & Blomhoff 2006, von Lintig et al. 2010, D'Ambrosio et al. 2011). This section describes the retinoid cycle in rods during dark/twilight conditions.

Literature references

Clugston, RD., Blaner, WS., D'Ambrosio, DN. (2011). Vitamin A metabolism: an update. *Nutrients, 3*, 63-103.

Kiser, PD., Golczak, M., von Lintig, J., Palczewski, K. (2010). The biochemical and structural basis for trans-to-cis isomerization of retinoids in the chemistry of vision. *Trends Biochem. Sci., 35*, 400-10.

Blomhoff, HK., Blomhoff, R. (2006). Overview of retinoid metabolism and function. *J. Neurobiol., 66*, 606-30.

von Lintig, J. (2012). Metabolism of carotenoids and retinoids related to vision. *J. Biol. Chem., 287*, 1627-34.

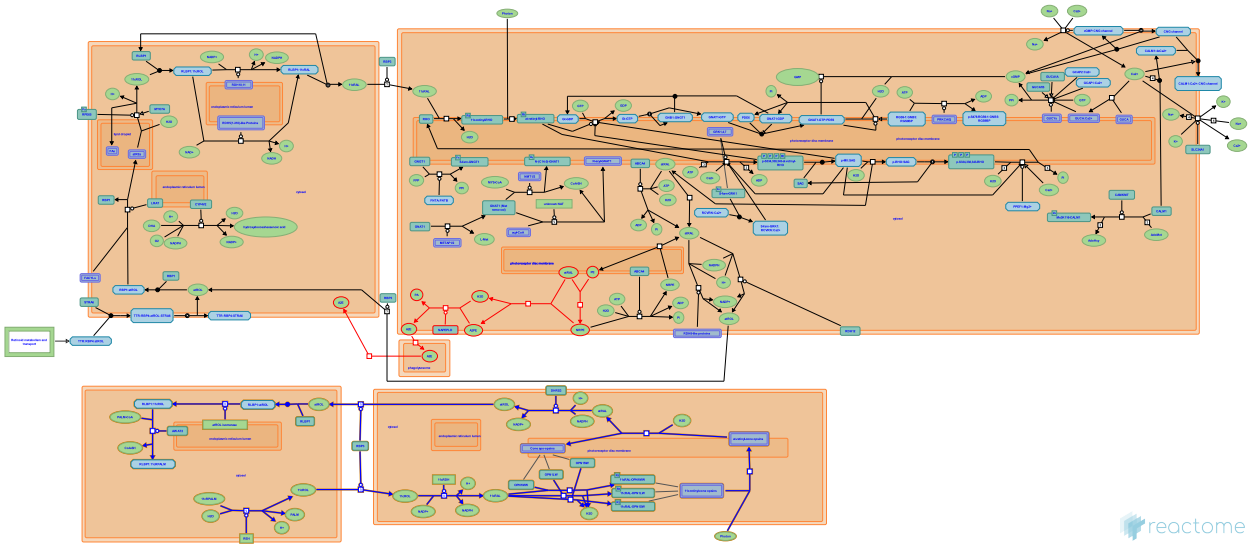
Editions

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

The retinoid cycle in cones (daylight vision) ↗

Location: Visual phototransduction

Stable identifier: R-HSA-2187335



Rods and cones share the same mechanism for the phototransduction process but perform functionally different roles. Although cone photoreceptors make up around 5% of all photoreceptor cells and are outnumbered 20 to 1 by rod photoreceptors, they mediate daylight vision in the human eye whereas rods mediate twilight vision. Also, cones are around 100-times less light-sensitive than rods thereby depriving us of colour vision in dark conditions in which cones cannot function. Rod function saturates in even moderate amounts of light whereas cones can adjust to even very bright light conditions, a process called light adaptation. In bright conditions, rods can take up to one hour to regain their sensitivity whereas cones can recover in a few minutes, a process called dark adaptation and which allows us to retain visual perception in changing light conditions.

Cone cells express three types of opsin which allow colour discrimination. Long Wavelength Sensitive Opsin (OPN1LW) detects red , Short Wavelength Sensitive Opsin (OPN1SW) detects blue, and Medium Wavelength Sensitive Opsin (OPN1MW) detects green regions of the light spectrum.

In the canonical retinoid (visual) cycle, the visual chromophore is regenerated in reactions involving the rod outer segments (ROS) and the retinal pigment epithelium (RPE). For cones, chromophore recycling is independent of the RPE and instead involves Muller cells in the retina which supply the chromophore selectively to cones. The molecular steps of the cone retinoid (visual) cycle are outlined in this section. The ability of cones to react to bright and differing light conditions means it has to regenerate the chromophore much quicker than rods. All-trans-retinol (atROL) released from cone outer segments is taken up by Muller cells where it is directly isomerized back to 11-cis-retinol (11cROL) then esterified by LRAT. When required, these 11-cis-retinyl esters can be hydrolysed by 11-cis-RE hydrolases back to 11cROL then oxidised in the cone photoreceptor cell to regenerate 11-cis-retinal (11cRAL), the visual chromophore (see reviews von Lintig 2012, Wang & Kefalov 2011, Kefalov 2012, Wolf 2004).

Literature references

Kefalov, VJ. (2012). Rod and cone visual pigments and phototransduction through pharmacological, genetic, and physiological approaches. *J. Biol. Chem., 287*, 1635-41. ↗

Kefalov, VJ., Wang, JS. (2011). The cone-specific visual cycle. *Prog Retin Eye Res, 30*, 115-28. ↗

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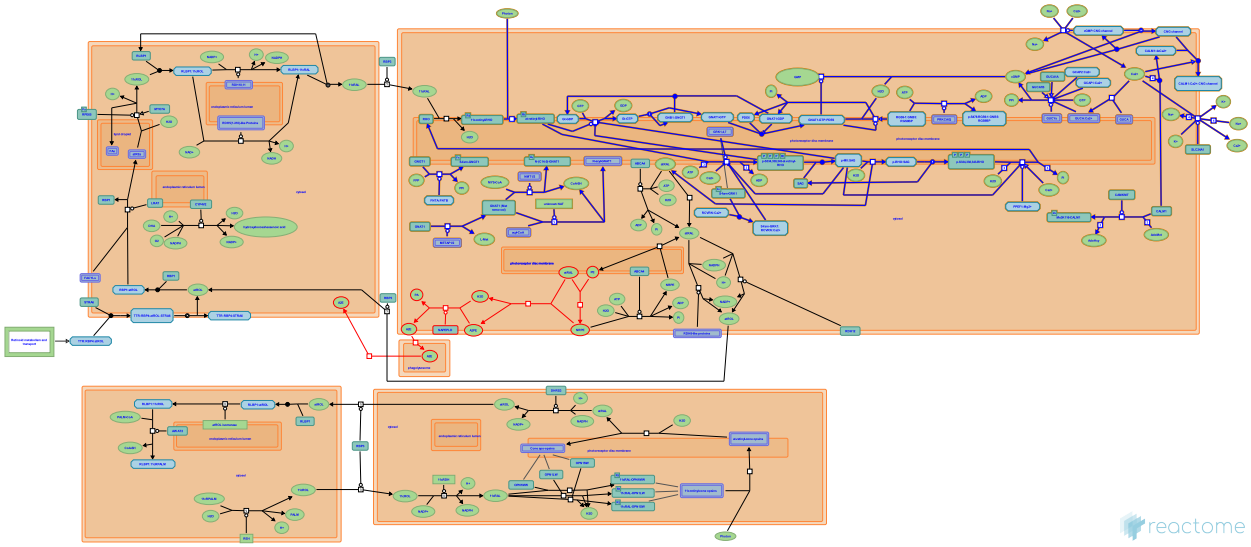
2013-01-31	Reviewed	Blaner, WS.

The phototransduction cascade ↗

Location: Visual phototransduction

Stable identifier: R-HSA-2514856



The visual pigment (rhodopsin in rods) consists of an 11-cis-retinal (11cRAL) chromophore covalently attached to a GPCR opsin family member via a Schiff base linkage. Upon photon absorption, 11cRAL isomerizes to all trans retinal (atRAL), changing the conformation of opsin to a form that can activate the regulatory G protein transducin (Gt). The alpha subunit of Gt activates phosphodiesterase which hydrolyses cGMP to 5'-GMP. A high level of cGMP keeps cGMP-gated cation channels open, so lower cGMP levels close these channels and hyperpolarize the cell. The hyperpolarization spreads passively to the synapse located at the opposite end of the rod, where it subsequently closes voltage-gated calcium channels. Vesicular release of the neurotransmitter glutamate subsides as the intracellular calcium levels drop. This diminution of neurotransmitter release relays the light signal to postsynaptic neurons. The events below describe activation, inactivation, recovery and regulation of the phototransduction cascade in rods (Burns & Pugh 2010, Korenbrot 2012, Smith 2010).

Literature references

Korenbrot, JI. (2012). Speed, sensitivity, and stability of the light response in rod and cone photoreceptors: facts and models. *Prog Retin Eye Res, 31*, 442-66. ↗

Pugh, EN., Burns, ME. (2010). Lessons from photoreceptors: turning off G-protein signaling in living cells. *Physiology (Bethesda), 25*, 72-84. ↗

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Editions

2012-10-11	Authored, Edited	Jassal, B.
2013-04-11	Reviewed	Makino, C.

Table of Contents