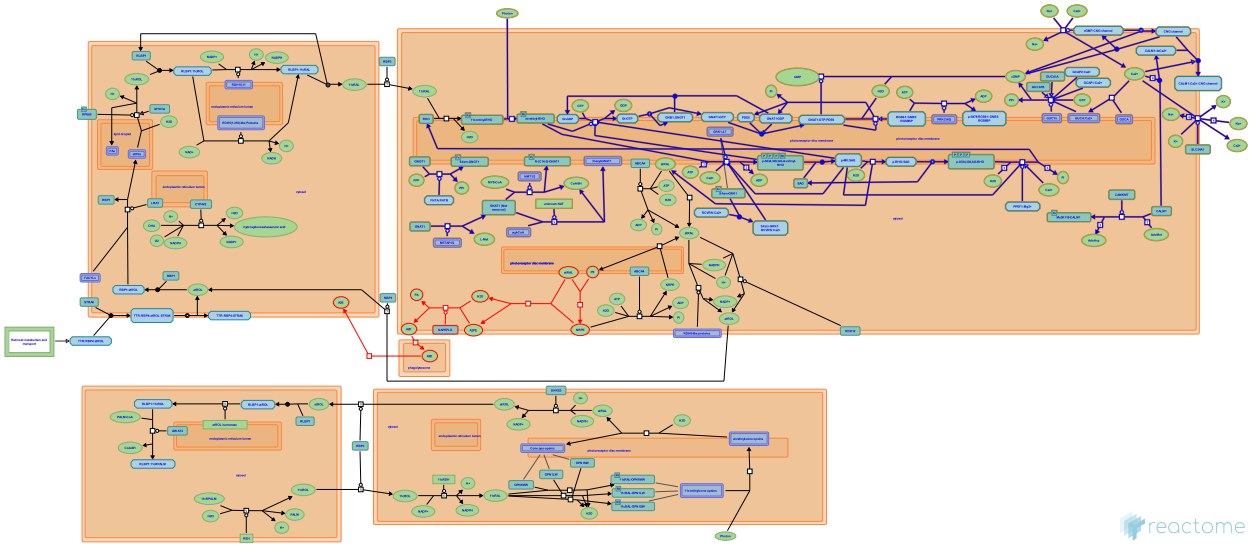
The phototransduction cascade



Jassal, B., Makino, C.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

06/05/2024

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. ↗

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. ↗

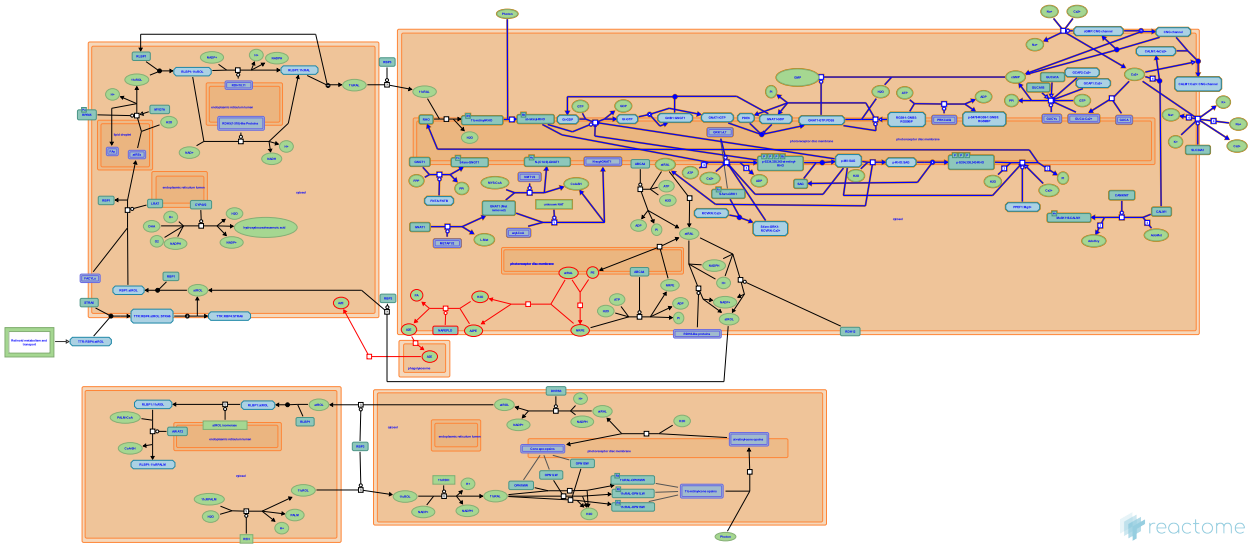
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

Reactome database release: 88

This document contains 3 pathways (see Table of Contents)

The phototransduction cascade ↗

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. ↗

Smith, SO. (2010). Structure and activation of the visual pigment rhodopsin. *Annu Rev Biophys, 39*, 309-28. ↗

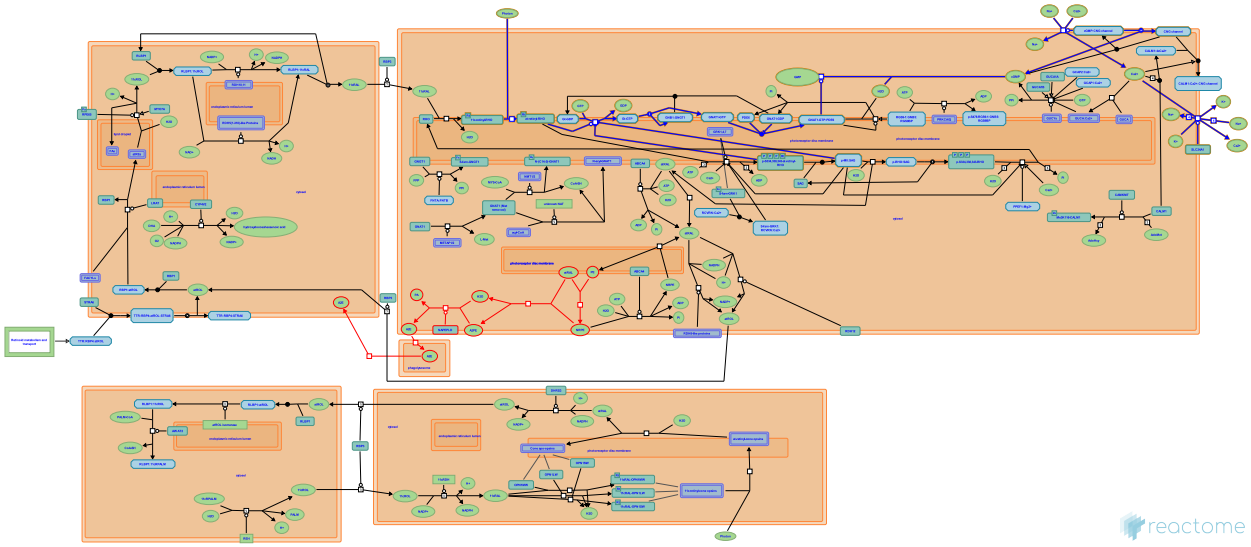
Editions

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

Activation of the phototransduction cascade ↗

Location: The phototransduction cascade

Stable identifier: R-HSA-2485179



The photoreceptor cascade starts with light isomerization of 11-cis-retinal (11cRAL) of rhodopsin (RHO) to all-trans-retinal (atRAL), inducing a conformational change in RHO to the active, metarhodopsin II (MII) state. MII activates the G protein transducin (Gt) that in turn activates phosphodiesterase 6 (PDE6). Consequently, there is a fall in the intracellular concentration of cGMP that closes cGMP-dependent cation channels (CNG channels) and hyperpolarizes the rod. This has the effect of reducing or stopping glutamate release from synaptic vesicles thus signalling to the surrounding cells how many photons were absorbed (Burns & Pugh 2010, Korenbrot 2012, Pugh & Lamb 1993).

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. ↗

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

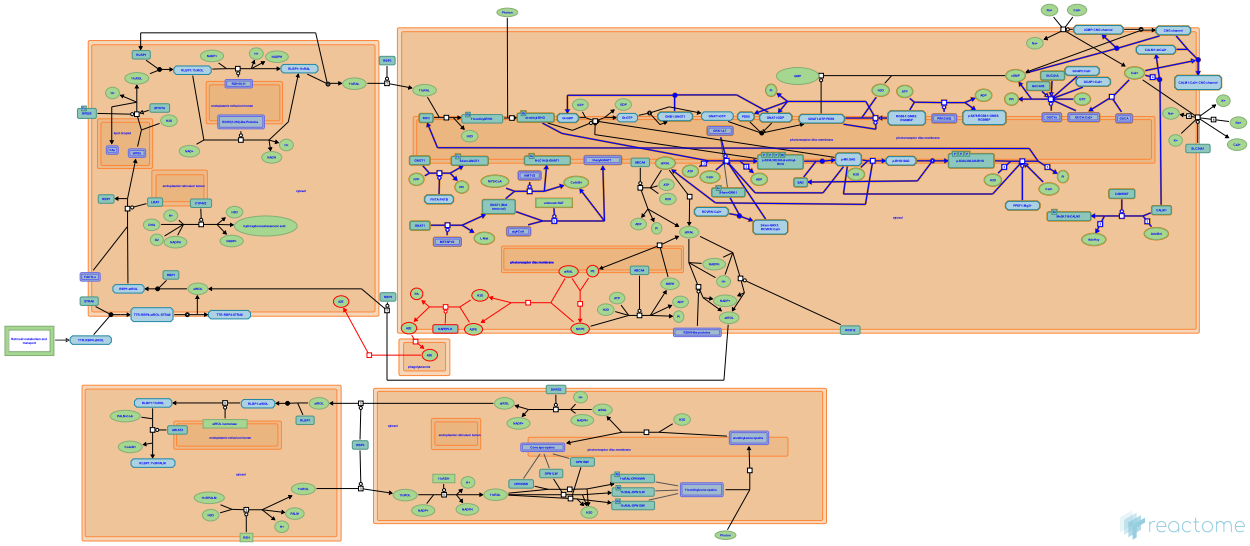
Editions

2012-10-01	Authored, Edited	Jassal, B.
2013-04-11	Reviewed	Makino, C.

Inactivation, recovery and regulation of the phototransduction cascade ↗

Location: The phototransduction cascade

Stable identifier: R-HSA-2514859



To terminate the single photon response and restore the system to its basal state, the three activated intermediates in phototransduction, rhodopsin (MII), transducin alpha subunit with GTP bound (GNAT1-GTP) and phosphodiesterase 6 (PDE6) all need to be efficiently deactivated. In addition, the cGMP concentrations must be restored to support reopening of the CNG channels. This section describes the inactivation and recovery events of the activated intermediates involved in phototransduction (Burns & Pugh 2010, Korenbrot 2012).

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. ↗

Editions

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

Table of Contents