GRK1,4,7 phosphorylate MII to p-MII

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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.

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Literature references

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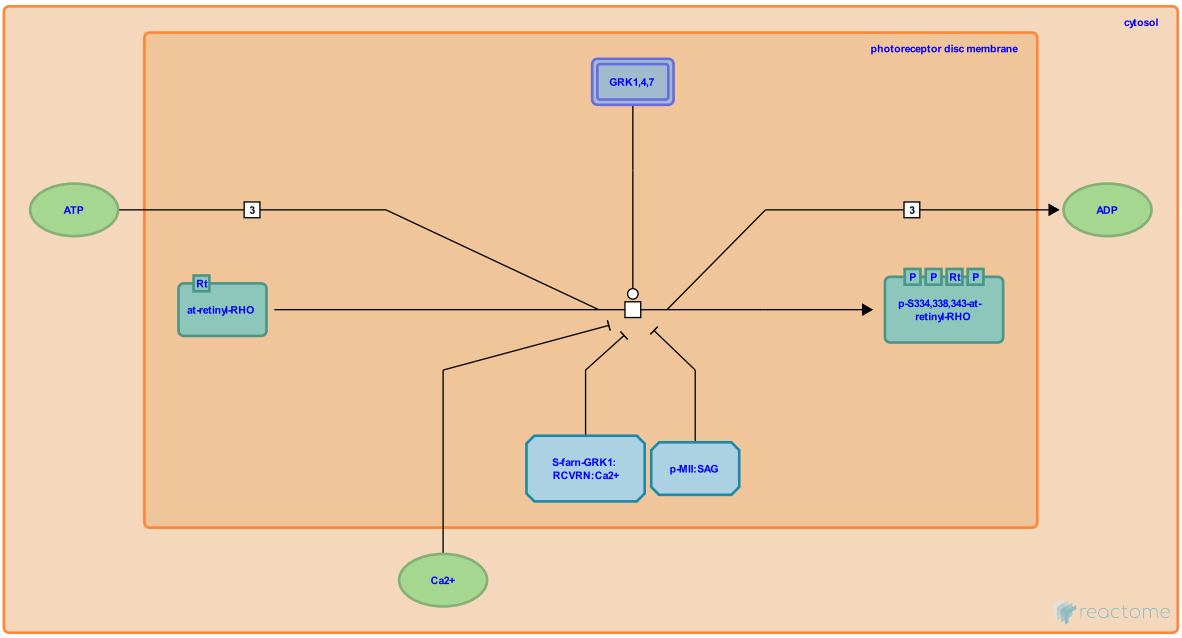
Stable identifier: R-HSA-2581474

Type: transition

Compartments: cytosol, photoreceptor disc membrane



Activated rhodopsin (MII aka R*) must be deactivated to terminate the single photon response. Deactivation begins during the rising phase of the single photon response after MII binds rhodopsin kinase (GRK1), a serine/threonine protein kinase (Khani et al. 1996). GRK1 is activated by MII whereupon it phosphorylates MII at multiple serine and threonine sites on its C terminus. There are six serine and threonine residues that can be phosphorylated. Increasing phosphorylation progressively reduces the rate at which MII can activate transducin but full quenching requires the binding of arrestin (S-antigen or SAG, Yamaki et al. 1988) which binds to and sterically caps MII (Burns & Pugh 2010, Korenbrot 2012). GRK4-alpha (isoform 1) and GRK7 are also able to phosphorylate rhodopsin thereby deactivating it (Premont et al. 1996, Chen et al. 2001, Horner et al. 2005, Osawa et al. 2008).

A substantial fraction of rhodopsin kinase (GRK1) is bound to recoverin (RCVRN) in darkness, when internal Ca2+ levels are high. RCVRN is an EF-hand protein (Murakami et al. 1992) that functions as a myristoyl switch. With Ca2+ bound, the myristoyl group is exposed to attach RCVRN to the membrane. When Ca2+ levels drop with light exposure, Ca2+ dissociates from RCVRN and GRK1 is released. Higher levels of free GRK1 accelerate the phosphorylation and shutoff of photoexcited rhodopsin (MII).

Certain mutations in GRK1 cause Oguchi type 2 disease, a rare, recessive form of congenital stationary night blindness (https://sph.uth.edu/retnet/).

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Editions

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