GNAT1-GTP hydrolyses its bound GTP to GDP

Jassal, B., Makino, C.

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

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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

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. ↗

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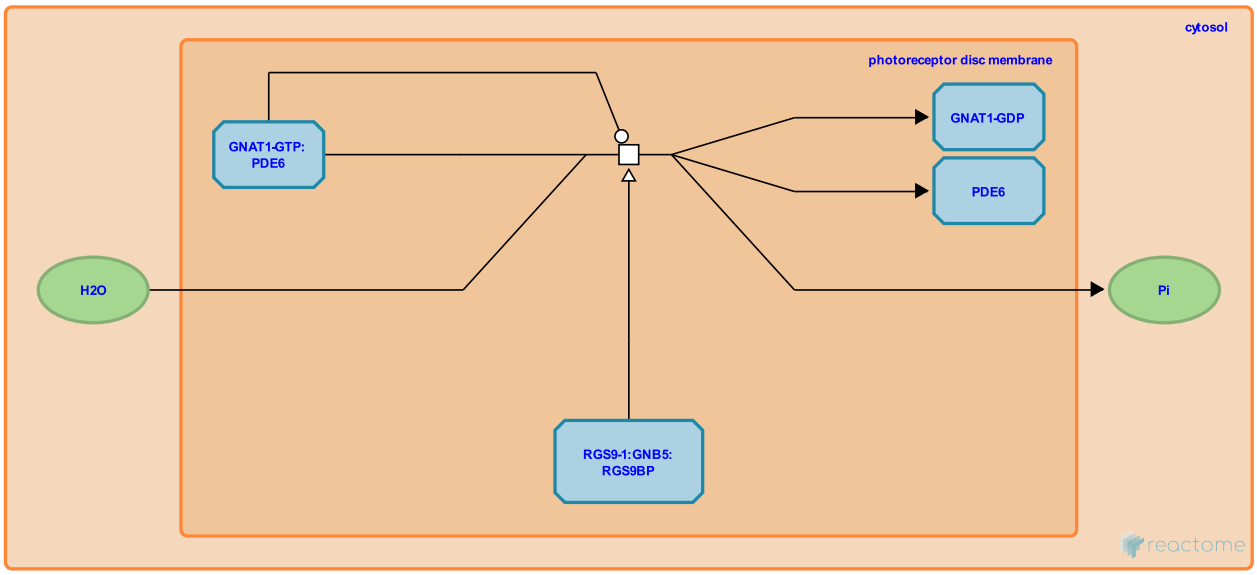
Stable identifier: R-HSA-2584246

Type: transition

Compartments: photoreceptor disc membrane, cytosol



Active Gt alpha (GNAT-GTP) can be inactivated by a slow, intrinsic GTPase activity that hydrolyses GTP to GDP. Once GNAT1 has GDP bound, it no longer binds to the gamma subunit of PDE6 (PDE6-gamma) that then resumes inhibition of the catalytic subunit of PDE6. The hydrolysis of GTP is accelerated by a GAP (GTPase accelerating protein) complex that consists of Regulator of G protein signaling 9 (RGS9-1, RGS9 isoform 3) (He et al. 1998, Zhang et al. 1999), Guanine nucleotide binding protein subunit beta 5, long form (GNB5) (Makino et al. 1999) and RGS9 anchoring protein (RGS9BP, aka R9AP) (Hu & Wensel 1998). The affinity of GNAT GTP for the GAP complex is relatively low, but is increased significantly by the presence of PDE-gamma. Shutoff of Gt is the rate-limiting step in the recovery of the single photon response of rods (Chen et al. 2000, Krispel et al. 2006). Persons with defective GAP experience bradyopsia or "slow vision" in which there are difficulties in adjusting to changes in brightness and to tracking moving objects (Michaelides et al. 2010, Nishiguchi et al. 2004).

Literature references

Hykin, PG., Webster, AR., Richardson, EC., Holder, GE., Moore, AT., Rana, NA. et al. (2010). Novel mutations and electrophysiologic findings in RGS9- and R9AP-associated retinal dysfunction (Bradyopsia). *Ophthalmology, 117*, 120-127.e1. ↗

Handy, JW., Arshavsky, VY., Li, T., Makino, ER. (1999). The GTPase activating factor for transducin in rod photoreceptors is the complex between RGS9 and type 5 G protein beta subunit. *Proc Natl Acad Sci U S A, 96*, 1947-52. ↗

Chen, CK., Chen, YJ., Chen, D., Arshavsky, VY., Martemyanov, KA., Burns, ME. et al. (2006). RGS expression rate-limits recovery of rod photoresponses. *Neuron, 51*, 409-16. ↗

Berson, EL., Hagstrom, SA., Nishiguchi, KM., Arshavsky, VY., Sandberg, MA., Pott, JW. et al. (2004). Defects in RGS9 or its anchor protein R9AP in patients with slow photoreceptor deactivation. *Nature, 427*, 75-8. ↗

Howes, KA., Pettenati, MJ., Zhang, K., Wensel, TG., Chen, C., Baehr, W. et al. (1999). Structure, alternative splicing, and expression of the human RGS9 gene. *Gene, 240*, 23-34. ↗

Editions

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