BESTs transport cytosolic Cl- to extracellular region

He, L., Jassal, B.

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. ↗

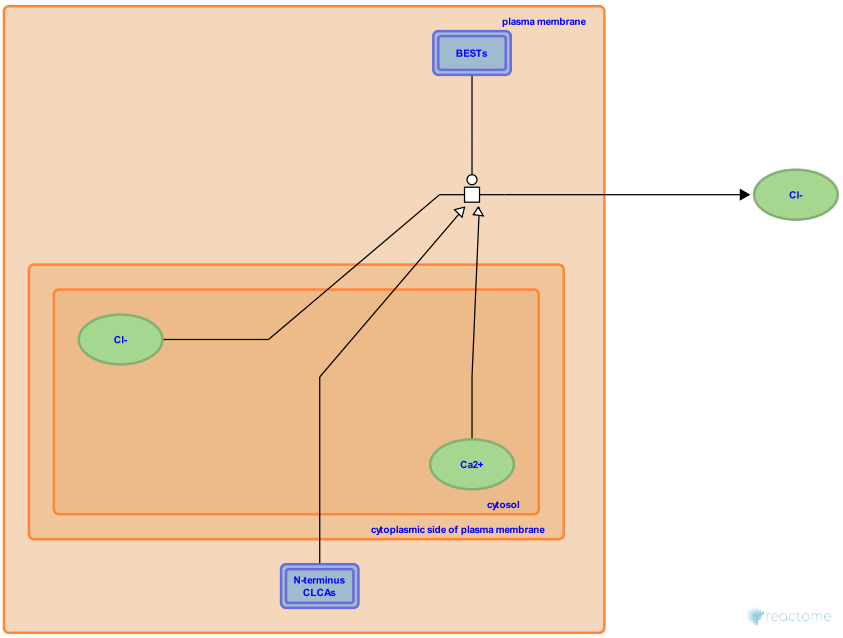
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

BESTs transport cytosolic Cl- to extracellular region ↗

Stable identifier: R-HSA-2744361

Type: transition

Compartments: cytosol, extracellular region, plasma membrane



Bestrophins 1-4 (BEST1-4, aka vitelliform macular dystrophy proteins) mediate cytosolic Cl- efflux across plasma membranes. This transport is sensitive to intracellular Ca2+ concentrations (Sun et al. 2002, Tsunenari et al. 2003). Mutations in bestrophins that impair their function are implicated in macular degeneration in the eye. Defects in BEST1 cause vitelliform macular dystrophy (BVMD, Best's disease, MIM:153700), an autosomal dominant form of macular degeneration that usually begins in childhood and is characterized lesions due to abnormal accumulation of lipofuscin within and beneath retinal pigment epithelium (RPE) cells (Marquardt et al. 1998, Petrukhin et al. 1998). All CLCAs contain a consensus cleavage motif which is recognised by an internal zincin metalloprotease domain within the N terminus. Self-proteolysis within the secretory pathway yields N- and C-terminal fragments, a step critical for CLCA activation of calcium-activated chloride channels (CaCCs) mediated through the N-terminal fragment (Yurtsever et al. 2012).

Literature references

Yau, KW., Sun, H., Nathans, J., Tsunenari, T. (2002). The vitelliform macular dystrophy protein defines a new family of chloride channels. *Proc. Natl. Acad. Sci. U.S.A., 99*, 4008-13. ↗

Li, W., Bergen, AA., Petrukhin, K., Austin, CP., Caskey, CT., Forsman, K. et al. (1998). Identification of the gene responsible for Best macular dystrophy. *Nat. Genet., 19*, 241-7. ↗

Yau, KW., Williams, J., Sun, H., Smallwood, P., Nathans, J., Tsunenari, T. et al. (2003). Structure-function analysis of the bestrophin family of anion channels. *J. Biol. Chem., 278*, 41114-25. ↗

Stöhr, H., Weber, BH., Rivera, A., Passmore, LA., Krämer, F., Marquardt, A. (1998). Mutations in a novel gene, VMD2, encoding a protein of unknown properties cause juvenile-onset vitelliform macular dystrophy (Best's disease). *Hum. Mol. Genet., 7*, 1517-25. ↗

Editions

2012-12-06	Authored, Edited	Jassal, B.
2013-01-28	Reviewed	He, L.
2015-02-11	Revised	Jassal, B.