cAMP activates EPAC1

Gillespie, ME., Hill, DP., May, B.

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

09/05/2024

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. ↗

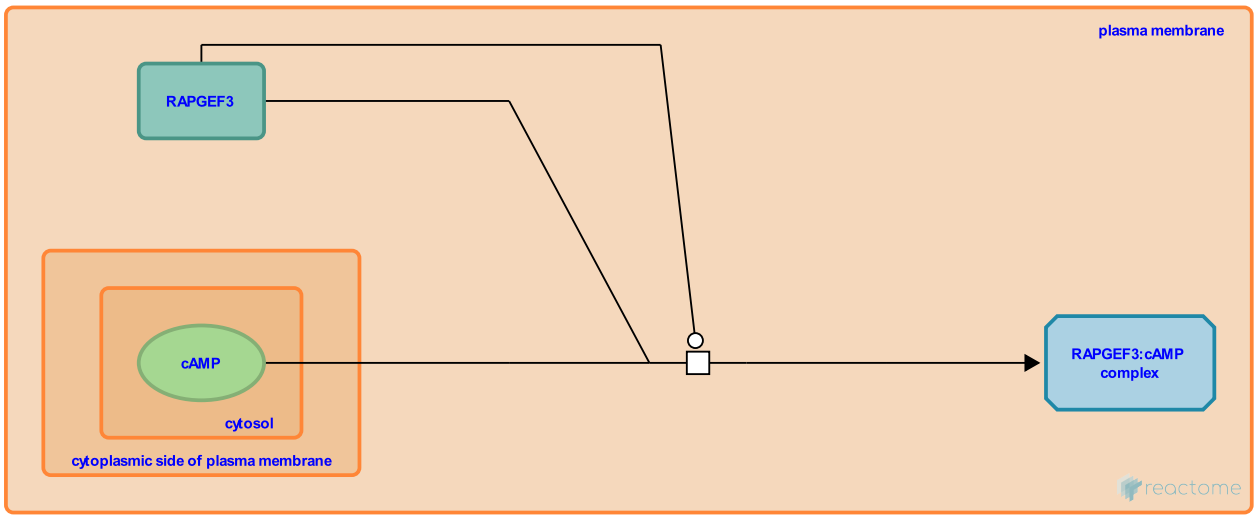
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

cAMP activates EPAC1 ↗

Stable identifier: R-HSA-381668

Type: transition

Compartments: plasma membrane, cytosol



Each molecule of RAPGEF3 / EPAC1 binds 1 molecule of cAMP. EPAC1 binds cAMP less tightly than PKA binds cAMP so it is believed that EPAC1 binds cAMP after PKA is saturated. The binding of cAMP by EPAC1 activates the guanyl nucleotide exchange activity of EPAC1. EPAC1 also binds the SUR1 subunit of ATP-gated potassium channels (KATP channels) in beta cells so EPAC1 may participate in direct regulation of potassium transport.
EPAC1 also interacts with the calcium sensor Piccolo in a complex with Rim2 at the cell membrane. This may influence exocytosis of insulin.

Literature references

Matsumoto, M., Yokoi, N., Tajima, N., Seino, S., Kashima, Y., Shibasaki, T. et al. (2002). Piccolo, a Ca2+ sensor in pancreatic beta-cells. Involvement of cAMP-GEFII.Rim2.Piccolo complex in cAMP-dependent exocytosis. *J Biol Chem, 277*, 50497-502. ↗

Brock, B., Gromada, J., Rorsman, P., Schmitz, O. (2004). Glucagon-like peptide-1: regulation of insulin secretion and therapeutic potential. *Basic Clin Pharmacol Toxicol, 95*, 252-62. ↗

Bos, JL., Monaco, M., Holz, GG., Chepurny, OG., Joseph, JW., Wheeler, MB. et al. (2003). Epac-selective cAMP analog 8-pCPT-2'-O-Me-cAMP as a stimulus for Ca2+-induced Ca2+ release and exocytosis in pancreatic beta-cells. *J Biol Chem, 278*, 8279-85. ↗

Chepurny, OG., Harbeck, M., Holz, GG., Roe, MW., Kang, G. (2006). Cell physiology of cAMP sensor Epac. *J Physiol, 577*, 5-15. ↗

Bos, JL., Malester, B., Holz, GG., Chepurny, OG., Rehmann, H., Rindler, MJ. et al. (2006). cAMP sensor Epac as a determinant of ATP-sensitive potassium channel activity in human pancreatic beta cells and rat INS-1 cells. *J Physiol, 573*, 595-609. ↗

Editions

2009-05-28	Authored, Edited	May, B.
2009-06-02	Reviewed	Gillespie, ME.
2024-02-12	Reviewed	Hill, DP.