CASTOR1 homodimer binds L-arginine and dissociates from GATOR2

Condon, KJ., Sabatini, DM.

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

11/05/2024

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. ↗

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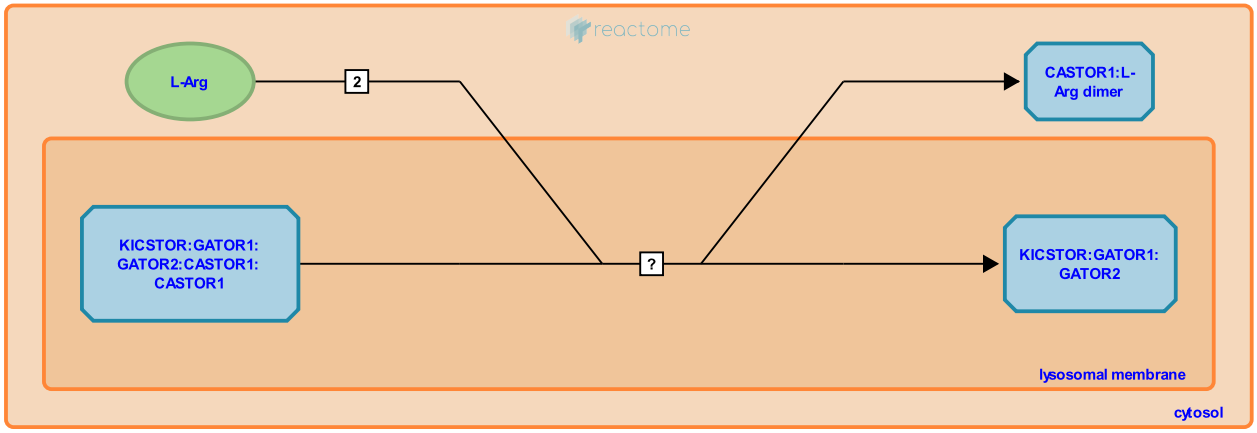
Stable identifier: R-HSA-9657619

Type: uncertain

Compartments: lysosomal membrane



The CASTOR1 homodimer interacts with the GATOR2 complex via the MIOS subunit of GATOR2 (Chantranupong et al. 2016, Gai et al. 2016). The ACT domains of CASTOR1 bind L-arginine (Chantranupong et al. 2016, Saxton et al. 2016, Xia et al. 2016, Gai et al. 2016) and CASTOR1:arginine dissociates from GATOR2, which then prevents GATOR1 from activating the GTPase of RRAGA,B (Chantranupong et al. 2016). GATOR1 is recruited to the lysosomal membrane by the KICSTOR complex (Wolfson et al. 2017).

Literature references

Sabatini, DM., Wang, T., Scaria, SM., Saxton, RA., Gygi, SP., Gygi, MP. et al. (2016). The CASTOR Proteins Are Arginine Sensors for the mTORC1 Pathway. *Cell, 165*, 153-164. ↗

Sabatini, DM., Petri, S., Condon, KJ., Shen, K., Orozco, JM., Scaria, SM. et al. (2017). KICSTOR recruits GATOR1 to the lysosome and is necessary for nutrients to regulate mTORC1. *Nature, 543*, 438-442. ↗

Ding, J., Wang, R., Zhang, T., Xia, J. (2016). Structural insight into the arginine-binding specificity of CASTOR1 in amino acid-dependent mTORC1 signaling. *Cell Discov, 2*, 16035. ↗

Yang, C., Wang, Q., Gai, Z., Deng, W., Wang, L., Wu, G. (2016). Structural mechanism for the arginine sensing and regulation of CASTOR1 in the mTORC1 signaling pathway. *Cell Discov, 2*, 16051. ↗

Sabatini, DM., Schwartz, TU., Saxton, RA., Chantranupong, L., Knockenhauer, KE. (2016). Mechanism of arginine sensing by CASTOR1 upstream of mTORC1. *Nature, 536*, 229-33. ↗

Editions

2019-08-08	Reviewed	Sabatini, DM., Condon, KJ.