reactome

Active MTORC1 phosphorylates ULK1

Jupe, S., Klionsky, DJ., Tooze, SA., Varusai, TM.

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

22/08/2021

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. ↗

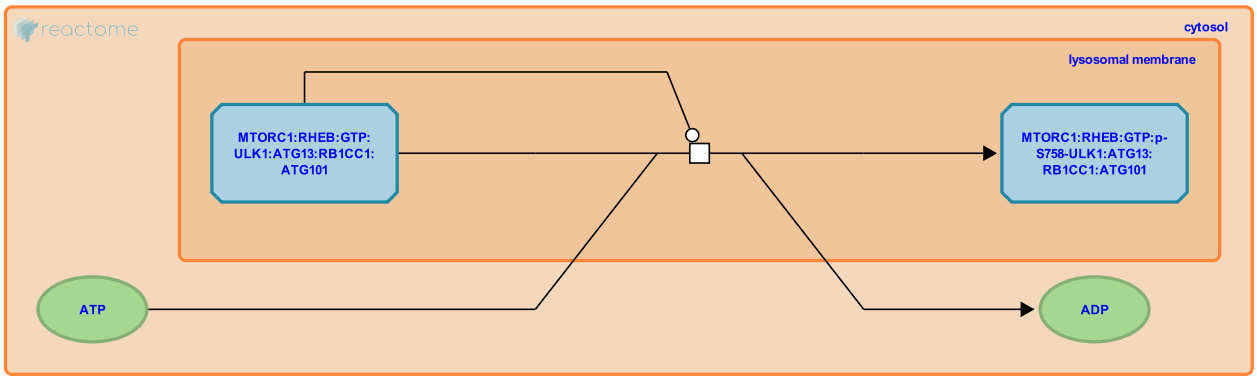
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

Active MTORC1 phosphorylates ULK1 ↗

Stable identifier: R-HSA-5672010

Type: transition

Compartments: lysosomal membrane



Under nutrient-rich conditions, mTORC1 phosphorylates ULK1 on S758 (Kim et al. 2011, Egan et al. 2011). ULK1 phosphorylation correlates with autophagy inhibition and reduced ULK1 kinase activity (Jung et al. 2009, Ganley et al. 2009, Hosakawa et al. 2009). RB1CC1 (FIP200) is probably phosphorylated (Mizushima 2010). ULK1 phosphorylation on S758 disrupts interaction between ULK1 and AMPK, thereby preventing AMPK from phosphorylating ULK1 at activating sites (Jung et al. 2009, Kim et al. 2011, Egan et al. 2011). If phosphorylation of ULK1 complex components suppresses autophagy, activation might be expected to involve more than suppression of kinases such as mTORC1. The phosphatase inhibitor okadaic acid inhibits autophagy (Blankson et al. 1995) but the protein phosphatase(s) involved in ULK1 dephosphorylation are currently unknown (Wong et al. 2013).

Literature references

Kim, J., Kundu, M., Viollet, B., Guan, KL. (2011). AMPK and mTOR regulate autophagy through direct phosphorylation of Ulk1. *Nat. Cell Biol., 13*, 132-41. ↗

Egan, D., Kim, J., Shaw, RJ., Guan, KL. (2011). The autophagy initiating kinase ULK1 is regulated via opposing phosphorylation by AMPK and mTOR. *Autophagy, 7*, 643-4. ↗

Editions

2015-02-02	Authored	Jupe, S.
2015-05-13	Edited	Jupe, S.
2015-05-13	Reviewed	Tooze, SA.
2015-09-03	Reviewed	Klionsky, DJ.
2019-03-05	Revised	Varusai, TM.