HSPA8 dissociates from LAMP2A-bound substrate

Metzakopian, E., Varusai, TM.

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

17/05/2024

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. ↗

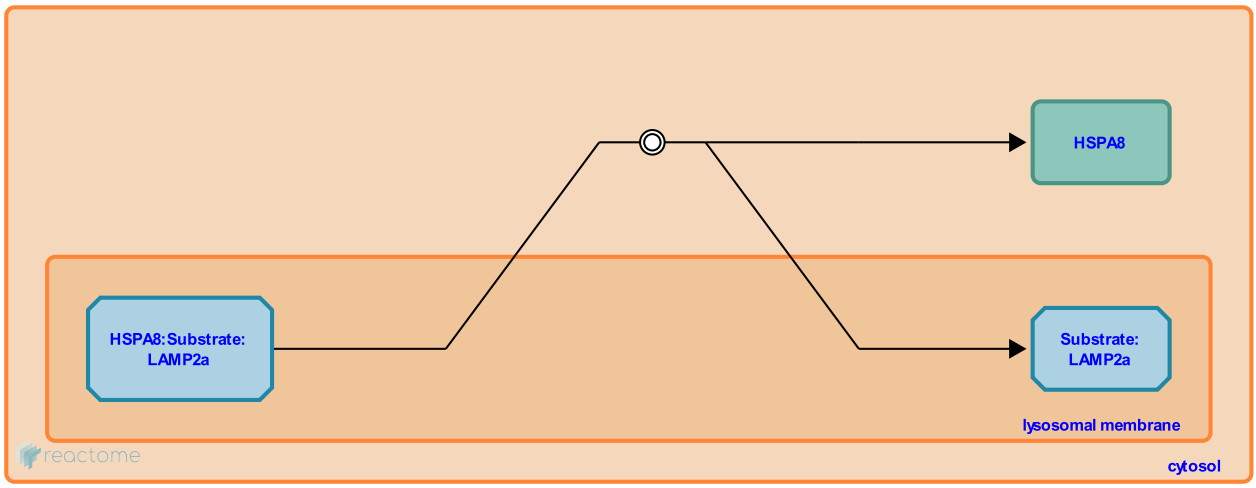
HSPA8 dissociates from LAMP2A-bound substrate ↗

Stable identifier: R-HSA-9622840

Type: dissociation

Compartments: cytosol, lysosomal membrane

Inferred from: Hspa8 dissociates from Lamp2a-bound substrate (Rattus norvegicus)



Intracellular proteins are targeted for proteolytic degradation in lysosome with the aid of chaperones. Heat shock cognate 71 kDa protein (HSPA8) acts as the constitutive chaperone that binds KFERQ-domain containing substrates in the cytosol. Consequently, the Hspa8:Substrate complex translocates from the cytosol to the lysosomal membrane where it binds to Lysosome-associated membrane glycoprotein 2 (LAMP2a). Post-binding, HSPA8 is released from the complex to allow multimerization of LAMP2a and internalization of the substrate (Bandyopadhyay U et al. 2008). Experiments confirming this binding were performed on rat models.

Literature references

Cuervo, AM., Kaushik, S., Bandyopadhyay, U., Varticovski, L. (2008). The chaperone-mediated autophagy receptor organizes in dynamic protein complexes at the lysosomal membrane. *Mol. Cell. Biol., 28*, 5747-63. ↗

Cuervo, AM., Kaushik, S. (2018). The coming of age of chaperone-mediated autophagy. *Nat. Rev. Mol. Cell Biol., 19*, 365-381. ↗

Editions

2019-02-21	Authored	Varusai, TM.
2019-02-22	Reviewed	Metzakopian, E.
2019-11-08	Edited	Varusai, TM.