Unfolded substrate in LAMP2a multimeric complex binds HSPA8

Metzakopian, E., Varusai, TM.

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

03/05/2024

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. ↗

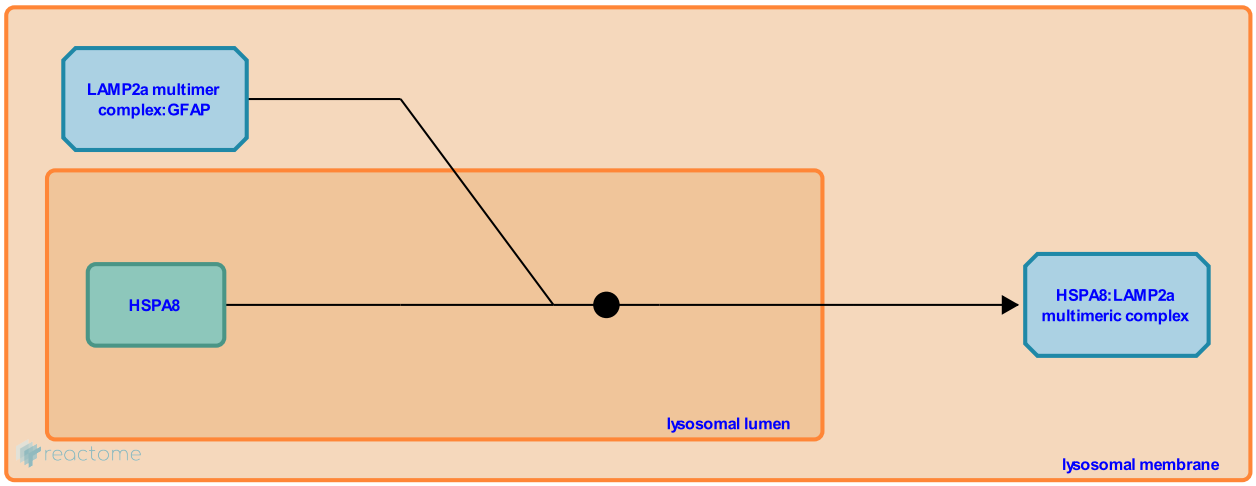
Unfolded substrate in LAMP2a multimeric complex binds HSPA8 ↗

Stable identifier: R-HSA-9625196

Type: binding

Compartments: lysosomal lumen, lysosomal membrane

Inferred from: Unfolded substrate in Lamp2 multimeric complex binds Hspa8 (Rattus norvegicus)



Intracellular proteins are targeted for proteolytic degradation in the lysosome with the aid of chaperones. Heat shock cognate 71 kDa protein (HSPA8) acts as the constitutive chaperone that binds a KFERQ-domain containing substrate in the cytosol and translocates to lysosomal membrane where it binds to Lysosome-associated membrane glycoprotein 2 (LAMP2a). Subsequently, Hspa8 is released and Heat shock protein HSP90 binds to the lysosomal luminal end of LAMP2a. The LAMP2a complex then multimerizes and stabilizes. Now, the substrate unfolds and binds to HSPA8 in the lysosomal lumen (Agarraberes FA et al. 1997, Cuervo AM et al. 1997). Subsequently, the substrate is internalized and degraded in the lumen. Experiments confirming this interaction were performed in rats.

Literature references

Dice, JF., Agarraberes, FA., Terlecky, SR. (1997). An intralysosomal hsp70 is required for a selective pathway of lysosomal protein degradation. *J. Cell Biol., 137*, 825-34. ↗

Dice, JF., Cuervo, AM., Knecht, E. (1997). A population of rat liver lysosomes responsible for the selective uptake and degradation of cytosolic proteins. *J. Biol. Chem., 272*, 5606-15. ↗

Editions

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