Late endosomal microautophagy

Metzakopian, E., Varusai, TM.

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

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of Creative Commons Attribution 4.0 International (CC BY 4.0) License. For more information see our license.

This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

17/11/2022
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


Reactome database release: 82

This document contains 1 pathway and 3 reactions (see Table of Contents)
Late endosomal microautophagy

Stable identifier: R-HSA-9615710

Compartments: cytosol, phagocytic vesicle

Microautophagy (MI) is a non-selective autophagic pathway that involves internalisation of cytosolic cargo through invaginations of the lysosomal membrane. MI can be induced by nitrogen starvation and complements other related self-eating processes such as Macroautophagy (MA) and Chaperone Mediated Autophagy (CMA). MI can degrade cell organelles and bulk cytosolic proteins directly via the lysosome and late endosome. MI can also target substrates with KFERQ motifs with the help of HSPA8 (Li W W et al. 2012).

Literature references

HSPA8 binds substrate

**Location:** Late endosomal microautophagy

**Stable identifier:** R-HSA-9615721

**Type:** binding

**Compartments:** cytosol

**Inferred from:** Hspa8 binds Rnase1 (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 substrate proteins in the cytosol. HSPA8 recognizes a motif based on the charge of the amino acids (Chiang H et al. 1989, Dice JF et al. 1990). This allows the motif to have multiple sequence possibilities and also create a motif through post-translational modifications such as phosphorylation and acetylation. Once bound with HSPA8, the substrates are targeted to the lysosome or endosome.

**Followed by:** HSPA8:substrate binds late endosomal phospholipids

**Literature references**


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019-02-21</td>
<td>Authored</td>
<td>Varusai, TM.</td>
</tr>
<tr>
<td>2019-02-22</td>
<td>Reviewed</td>
<td>Metzakopian, E.</td>
</tr>
<tr>
<td>2019-11-08</td>
<td>Edited</td>
<td>Varusai, TM.</td>
</tr>
</tbody>
</table>
HSPA8:substrate binds late endosomal phospholipids

**Location:** Late endosomal microautophagy

**Stable identifier:** R-HSA-9631068

**Type:** binding

**Compartments:** late endosome membrane, cytosol

**Inferred from:** Hspa8:substrate binds late endosomal phospholipids (Mus musculus)

Microautophagy (MI) can target KFERQ motif containing protein substrates to endosomal degradation. Upon binding with HSPA8, substrates are transported from the cytosol to late endosomes. Here, HSPA8 binds with the phospholipids on the late endosomal membrane. This interaction facilitates the vesicle-mediated transport of HSPA8:substrate complex into the late endosomes for degradation (Sahu R et al. 2011). Experiments confirming this interaction were performed in mouse cells.

**Preceded by:** HSPA8 binds substrate

**Followed by:** Substrate translocates into late endosomal lumen

**Literature references**


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019-02-21</td>
<td>Authored</td>
<td>Varusai, TM.</td>
</tr>
<tr>
<td>2019-02-22</td>
<td>Reviewed</td>
<td>Metzakopian, E.</td>
</tr>
<tr>
<td>2019-11-08</td>
<td>Edited</td>
<td>Varusai, TM.</td>
</tr>
</tbody>
</table>
**Substrate translocates into late endosomal lumen**

**Location:** Late endosomal microautophagy

**Stable identifier:** R-HSA-9631065

**Type:** transition

**Compartments:** late endosome membrane, late endosome lumen, cytosol

**Inferred from:** Substrate translocates into late endosomal lumen (Mus musculus)

In addition to bulk protein degradation, Microautophagy (MI) can also target KFERQ motif protein substrates similar to Chaperone Mediated Autophagy (CMA). However, MI is distinct from CMA in that it occurs during late endosomes/multivesicular bodies formation. Upon binding with Hspa8, substrates are transported from the cytosol to late endosomes. HSPA8 binds with the phospholipids on the late endosomal membrane. Subsequently, the substrate is transported into the lumen via endosomal sorting complexes required for transport (ESCRTI and ESCRTIII systems) (Sahu R et al. 2011). This event is represented as a black box since the precise molecular mechanism of the substrate transport into the endosomal lumen is unclear. Experiments confirming this event were performed in mouse.

**Preceded by:** HSPA8:substrate binds late endosomal phospholipids

**Literature references**


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019-02-21</td>
<td>Authored</td>
<td>Varusai, TM.</td>
</tr>
<tr>
<td>2019-02-22</td>
<td>Reviewed</td>
<td>Metzakopian, E.</td>
</tr>
<tr>
<td>2019-11-08</td>
<td>Edited</td>
<td>Varusai, TM.</td>
</tr>
</tbody>
</table>

https://reactome.org
Table of Contents

Introduction 1

Late endosomal microautophagy 2

HSPA8 binds substrate 3

HSPA8:substrate binds late endosomal phospholipids 4

Substrate translocates into late endosomal lumen 5

Table of Contents 6