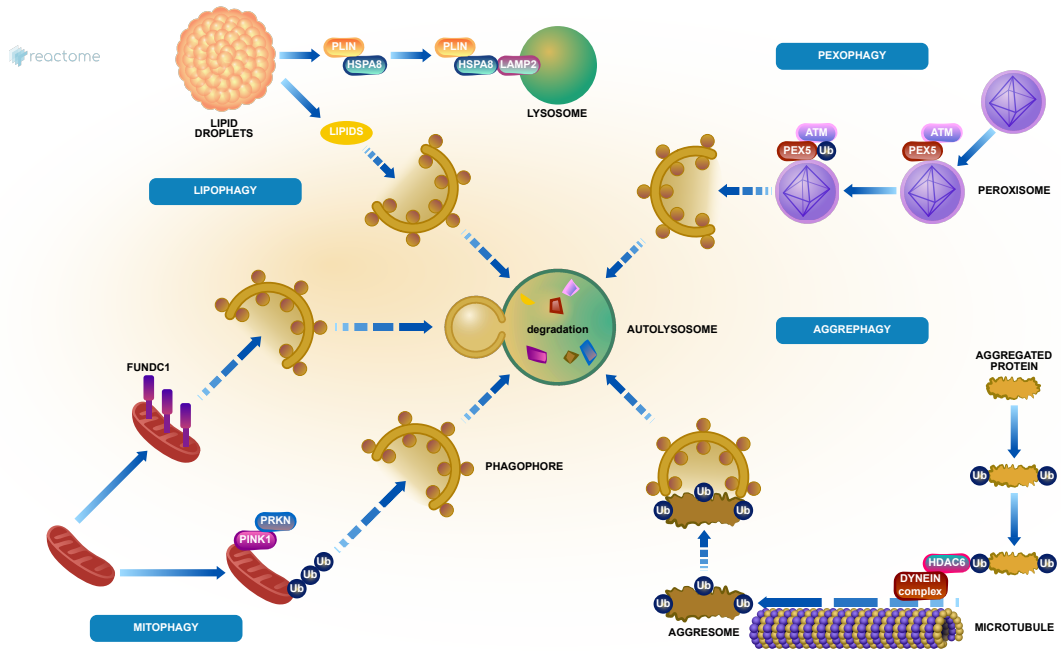
Selective autophagy



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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. ↗

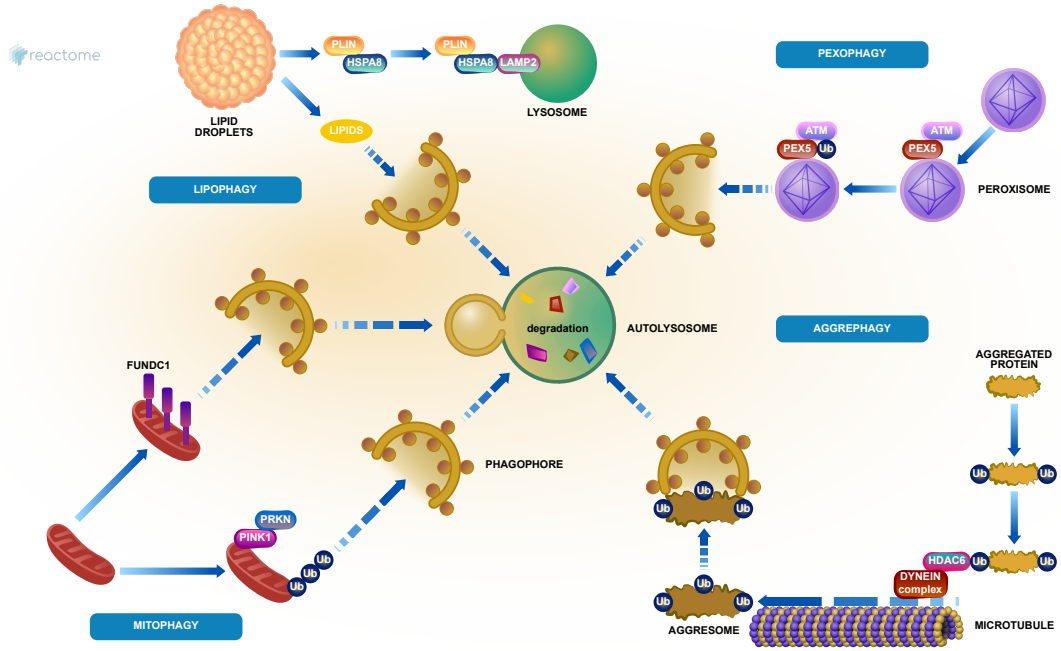
Reactome database release: 88

This document contains 5 pathways (see Table of Contents)

Selective autophagy

Stable identifier: R-HSA-9663891

Compartments: autophagosome, autophagosome membrane, cytosol, lysosomal lumen, lysosomal membrane, phagocytic vesicle, phagocytic vesicle membrane, phagophore assembly site membrane



Autophagy can be a selective process where specific cargo (organelles/proteins) are targetted to degradation in the lysosome. In general, selective autophagy is initiated when a cellular signal tags the cargo organelle for degradation. Subsequently, cargo recognition proteins detect and recruit the organelle to interact directly or indirectly with Atg proteins forming the phagophore. The next steps involve formation of the autophagosome and fusion with the lysosome for degradation. Depending upon the organelle, different molecules are used to for the autophagy mechanism (Andling AL et al. 2017). Consequently, the different mechanisms are known by the organelle degraded such as mitophagy for mitochondia, lipophagy for lipid droplets, pexophagy for peroxisomes and aggrephagy for aggregated proteins.

Literature references

Anding, AL., Baehrecke, EH. (2017). Cleaning House: Selective Autophagy of Organelles. *Dev. Cell, 41*, 10-22.

Editions

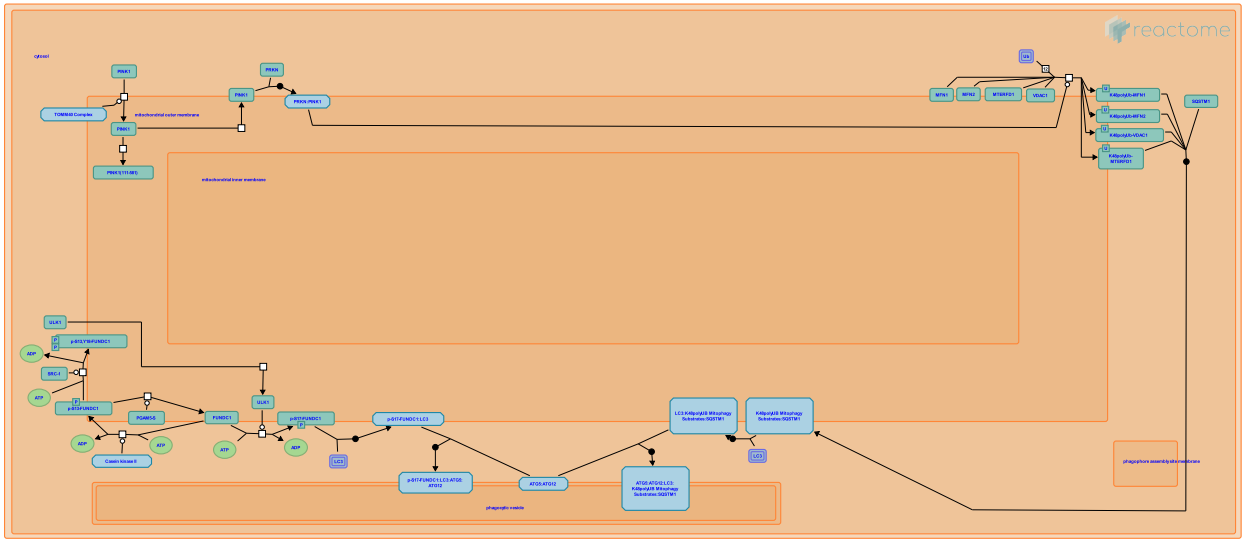
2019-11-08	Authored, Edited	Varusai, TM.

Mitophagy ↗

Location: Selective autophagy

Stable identifier: R-HSA-5205647

Compartments: cytosol



Mitophagy is a specific form of autophagy where mitochondria are specifically targeted for degradation by autophagolysosomes. In mammals there are a number of known mechanisms of mitophagy. One ensures maternal inheritance of mitochondrial DNA through the elimination of sperm derived mitochondria. A second is elimination of functional mitochondria during erythrocyte maturation and eye lens maturation. It is established that the outer mitochondrial membrane receptor Nix (or Bnip3l) and autophagosome associated protein LC3 are important for mitochondrial degradation in erythrocytes. A third mechanism is driven by the PINK1 and Parkin (PRKN) proteins. PRKN is recruited to the mitochondria when the mitochondrial membrane potential is reduced due to uncoupling, thereby initiating mitophagy.

Literature references

Narendra, DP., Youle, RJ. (2011). Mechanisms of mitophagy. *Nat. Rev. Mol. Cell Biol., 12*, 9-14. ↗

Editions

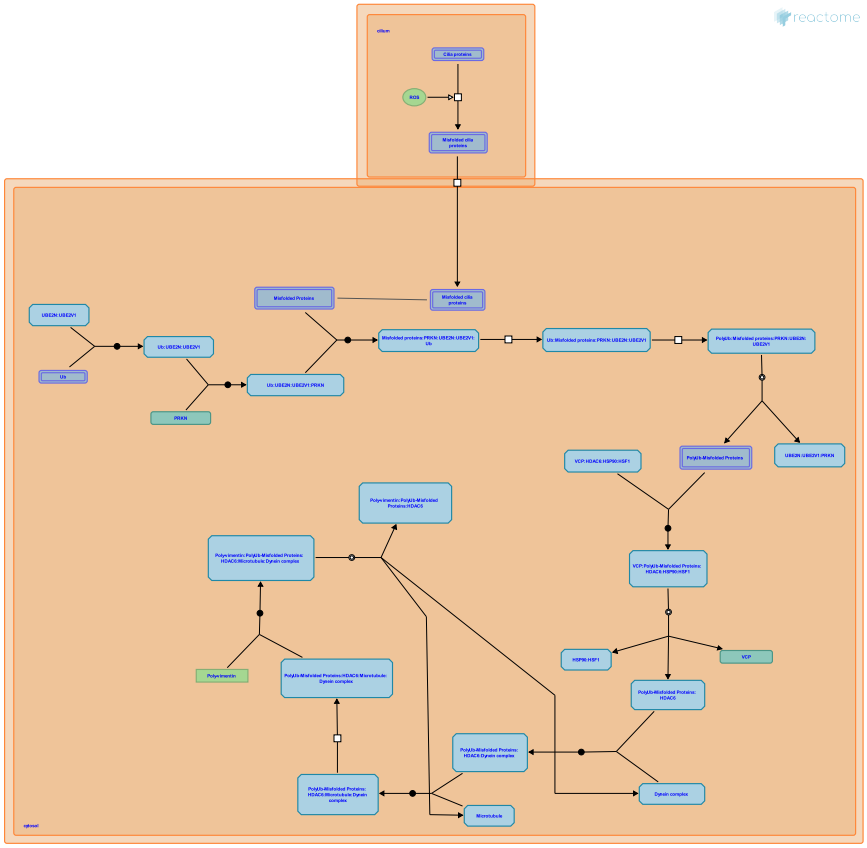
2013-11-21	Authored, Edited	Gillespie, ME.
2019-03-05	Revised	Varusai, TM.

Aggrephagy ↗

Location: Selective autophagy

Stable identifier: R-HSA-9646399

Compartments: cytosol



When the capacity of the proteosome to degrade misfolded proteins is limited, the alternate route to eliminate denatured proteins is via forming aggresomes - a process known as aggrephagy. Aggresome formation starts with ubiquitination of misfolded proteins following transport to the microtubule-organizing center (MTOC) with the help of dynein motor proteins. At the MTOC the cargo is encapsulated with intermediate filament proteins to result in the aggresome. Subsequently, this aggresome recruits chaperones that result in its autophagic elimination (Garcia Mata R et al. 2002).

Literature references

Gao, YS., Sztul, E., Garcia-Mata, R. (2002). Hassles with taking out the garbage: aggravating aggresomes. *Traffic, 3*, 388-96. ↗

Editions

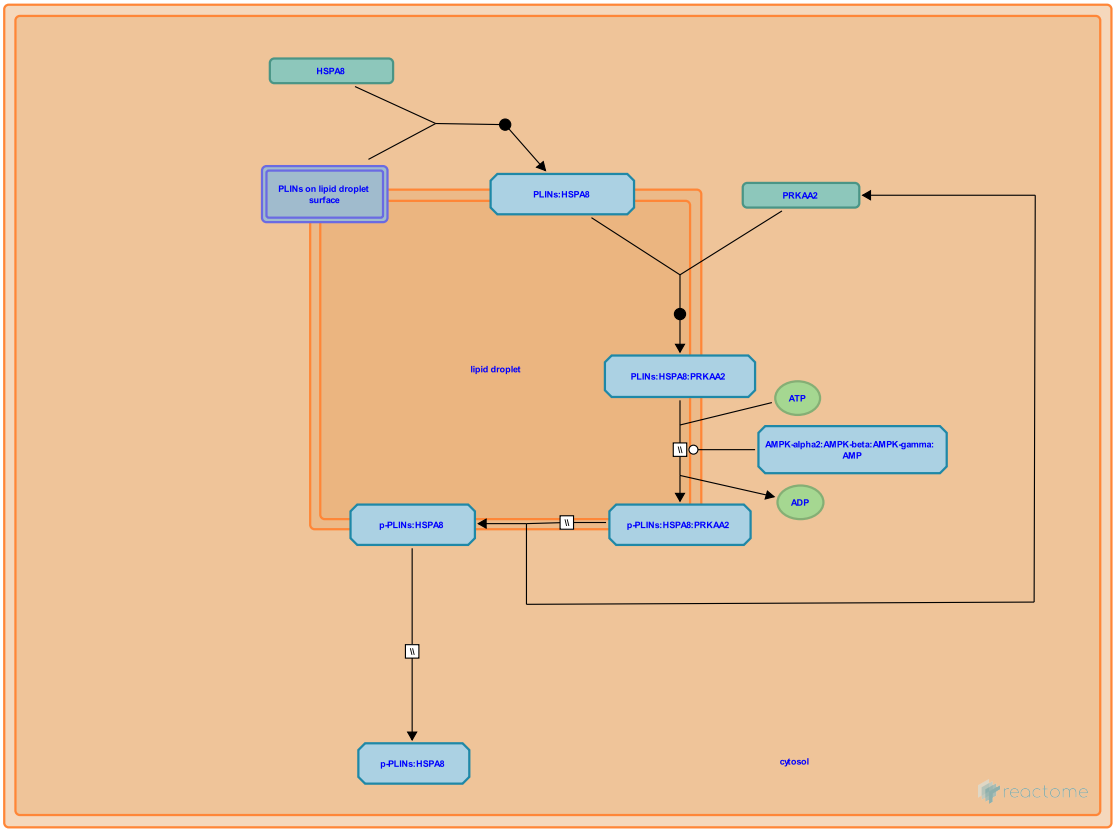
2019-05-23	Authored	Varusai, TM.
2019-05-24	Reviewed	Metzakopian, E.
2019-11-08	Edited	Varusai, TM.

Lipophagy ↗

Location: Selective autophagy

Stable identifier: R-HSA-9613354

Compartments: phagophore assembly site membrane, phagocytic vesicle, lysosomal lumen, autophagosome membrane, phagocytic vesicle membrane, cytosol, lysosomal membrane, autophagosome



Triglycerides stored in lipid droplets are hydrolysed under nutrient starvation to release fatty acids for energy. The content of lipid droplets may vary but they are all coated with a protective protein called perilipin. When this protein is degraded, lipid droplets associate with autophagic components and breakdown into fatty acids (Ward C et al. 2016, Schulze R J et al. 2017). This process is termed as lipophagy (Singh R et al. 2009).

Literature references

Czaja, MJ., Cuervo, AM., Novak, I., Komatsu, M., Tanaka, K., Kaushik, S. et al. (2009). Autophagy regulates lipid metabolism. *Nature, 458*, 1131-5. ↗

Mashek, DG., Sathyanarayan, A., Schulze, RJ. (2017). Breaking fat: The regulation and mechanisms of lipophagy. *Biochim. Biophys. Acta, 1862*, 1178-1187. ↗

Ward, C., Martinez-Lopez, N., Carroll, B., Maetzel, D., Singh, R., Korolchuk, VI. et al. (2016). Autophagy, lipophagy and lysosomal lipid storage disorders. *Biochim. Biophys. Acta, 1861*, 269-84. ↗

Editions

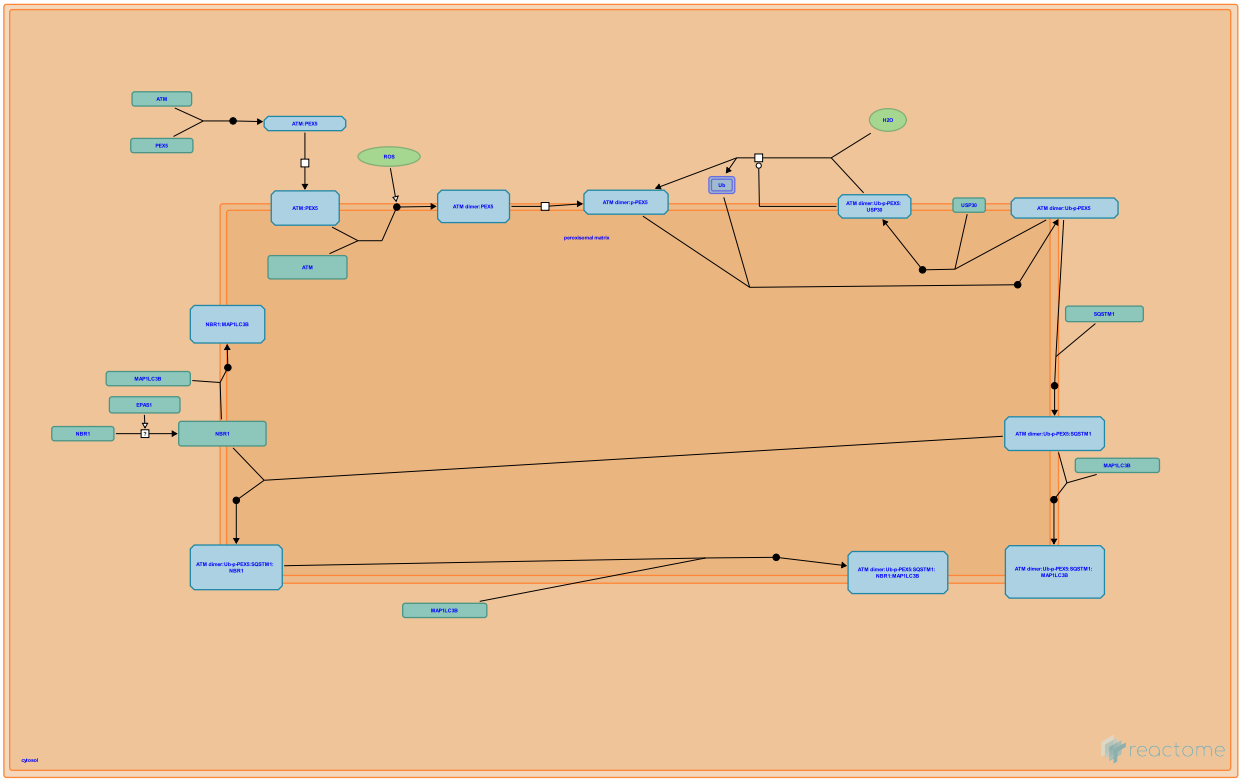
2019-02-21	Authored	Varusai, TM.
2019-02-22	Reviewed	Metzakopian, E.
2019-11-08	Edited	Varusai, TM.

Pexophagy ↗

Location: Selective autophagy

Stable identifier: R-HSA-9664873

Compartments: peroxisomal membrane, cytosol



Peroxisomes are cytosolic organelles involved in the catabolism of branched and long-chain fatty acids and in the reduction of reactive oxygen species (ROS). Peroxisomes homeostasis is critical to maintain ROS levels. Consequently, it is important to eliminate dysfunctional peroxisomes. The degradation of peroxisomes by autophagy is known as pexophagy (Katarzyna ZR et al. 2016). Pexophagy can be triggered by a shift in nutrient conditions.

Literature references

Subramani, S., Zientara-Rytter, K. (2016). Autophagic degradation of peroxisomes in mammals. *Biochem. Soc. Trans., 44*, 431-40. ↗

Editions

2019-10-29	Authored, Edited	Varusai, TM.
2019-10-30	Reviewed	Metzakopian, E.

Table of Contents