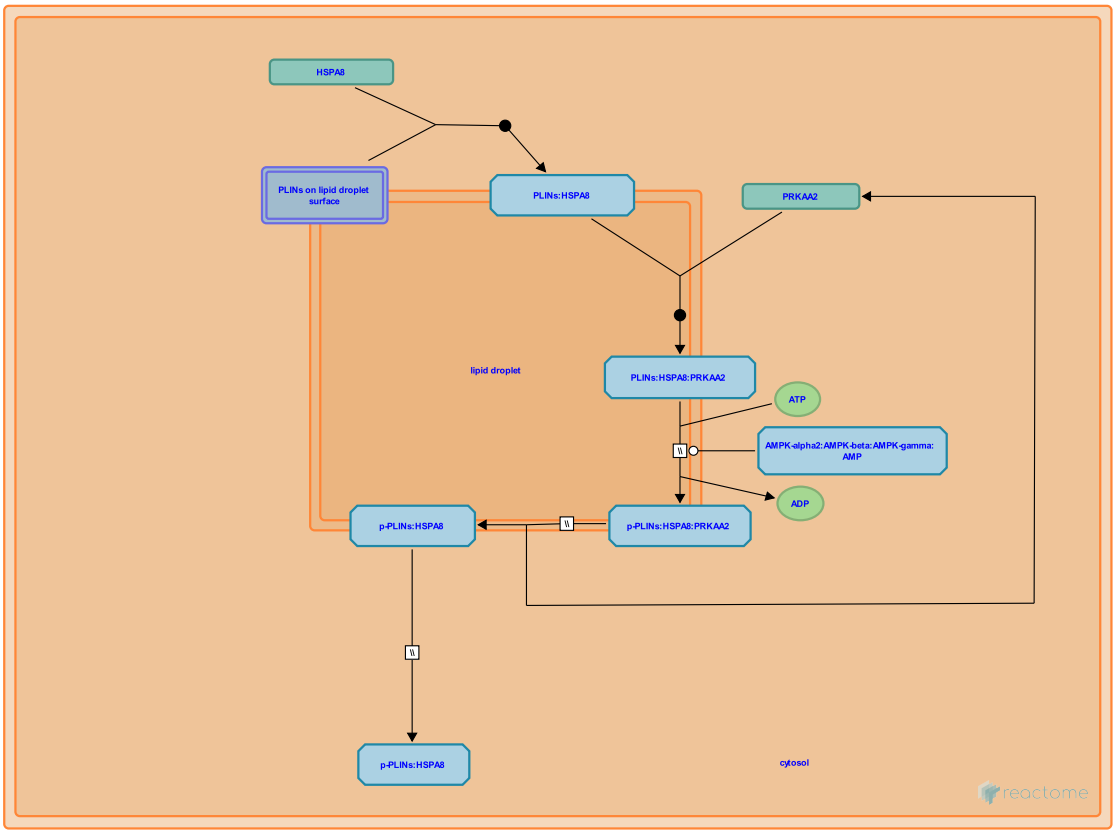
Lipophagy



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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. ↗

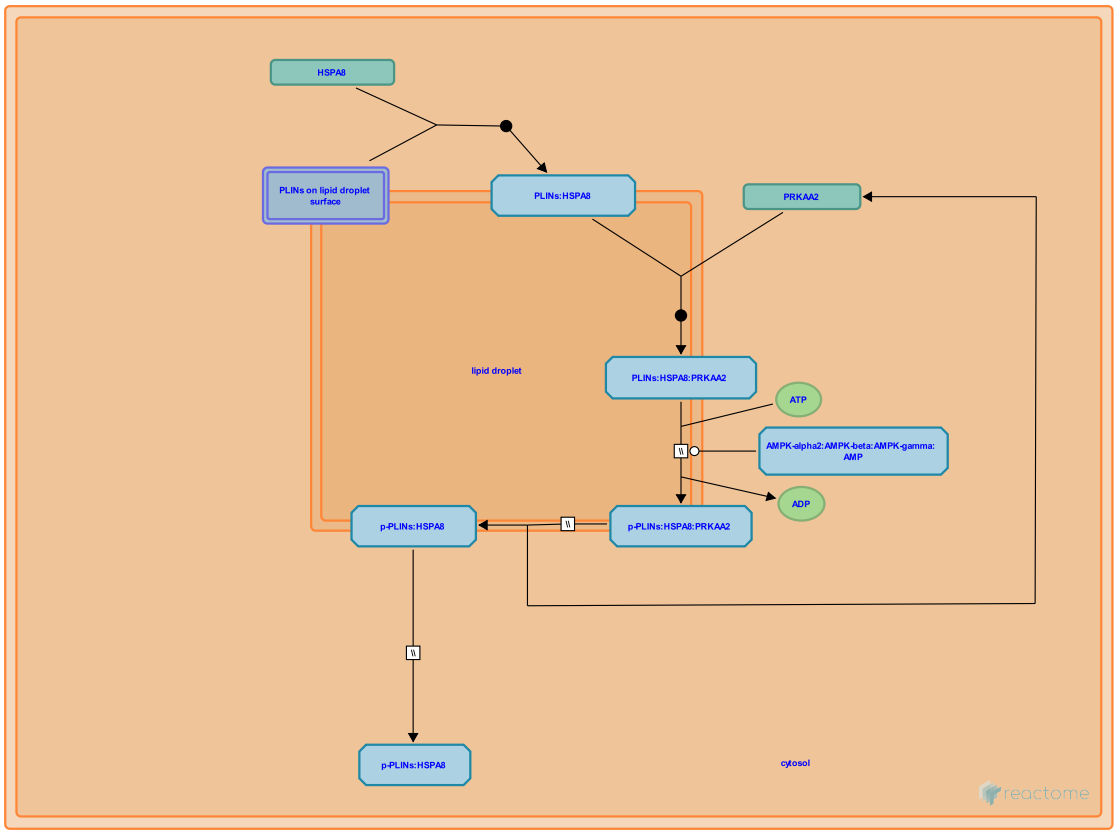
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Lipophagy ↗

Stable identifier: R-HSA-9613354

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



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.

PLINs bind HSPA8 ↗

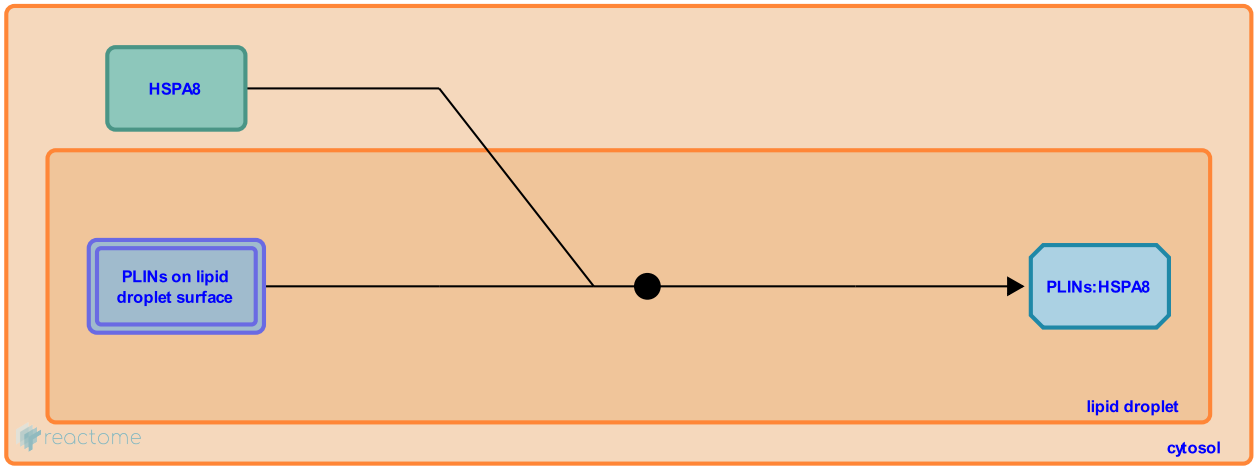
Location: Lipophagy

Stable identifier: R-HSA-9613352

Type: binding

Compartments: lipid droplet, cytosol

Inferred from: Plins bind Hspa8 (Rattus norvegicus)



Lipophagy is the process of autophagic degradation of lipid droplets into fatty acids. A key step in this process is the elimination of perilipin (PLIN) proteins on lipid droplet surface. This mechanism is initiated when the cytosolic Heat shock cognate 71 kDa protein (HSPA8) binds PLIN2 and PLIN3 on the lipid droplet surface. Consequently, perilipins are phosphorylated and targeted to degradation making the lipid available for hydrolysis (S Kaushik et al. 2015). Experiments confirming this interaction were performed in rats.

Followed by: PLINs:HSPA8 binds PRKAA2

Literature references

Cuervo, AM., Kaushik, S. (2015). Degradation of lipid droplet-associated proteins by chaperone-mediated autophagy facilitates lipolysis. *Nat. Cell Biol., 17*, 759-70. ↗

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PLINs:HSPA8 binds PRKAA2 ↗

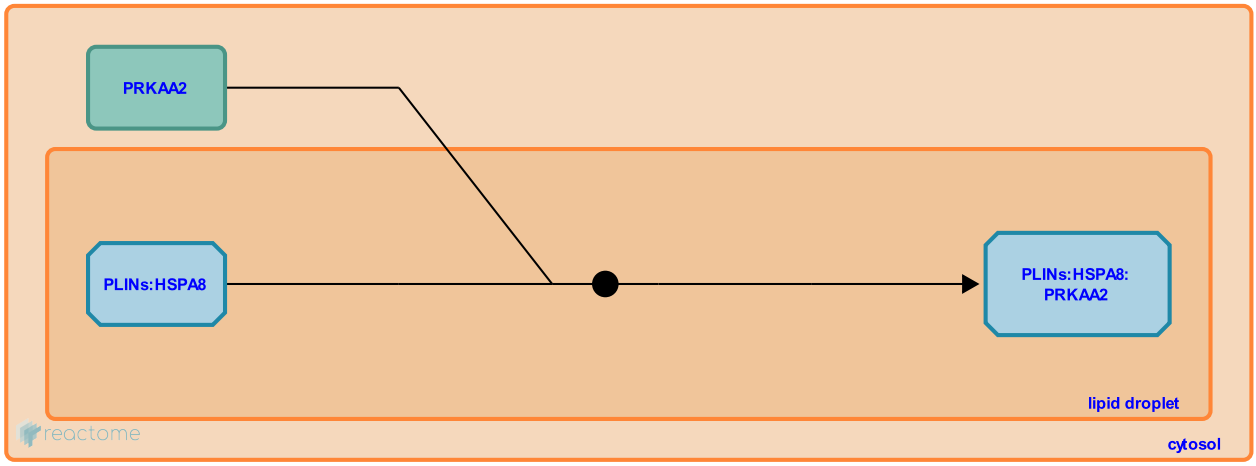
Location: Lipophagy

Stable identifier: R-HSA-9613513

Type: binding

Compartments: lipid droplet, cytosol

Inferred from: Plins:Hspa8 binds Prkaa2 (Mus musculus)



Lipophagy is the process of autophagic degradation of lipid droplets into fatty acids. Lipid droplets are coated with perilipin (PLIN) protiens and they need to be eliminated for the degradation of the lipids inside. Cytosolic Heat shock cognate 71 kDa protein (HSPA8) binds PLIN2 and PLIN3 on the lipid droplet surface. Consequently, PRKAA2 bind and phosphorylate perilipins targeting them for lipophagy (S Kaushik et al. 2015, S Kaushik et al. 2016). Experiments confirming this interaction were performed in mouse.

Preceded by: PRKAA2 dissociate from p-PLINs:HSPA8, PLINs bind HSPA8

Followed by: PRKAA2 phosphorylates PLINs

Literature references

Cuervo, AM., Kaushik, S. (2016). AMPK-dependent phosphorylation of lipid droplet protein PLIN2 triggers its degradation by CMA. *Autophagy, 12*, 432-8. ↗

Cuervo, AM., Kaushik, S. (2015). Degradation of lipid droplet-associated proteins by chaperone-mediated autophagy facilitates lipolysis. *Nat. Cell Biol., 17*, 759-70. ↗

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PRKAA2 phosphorylates PLINs ↗

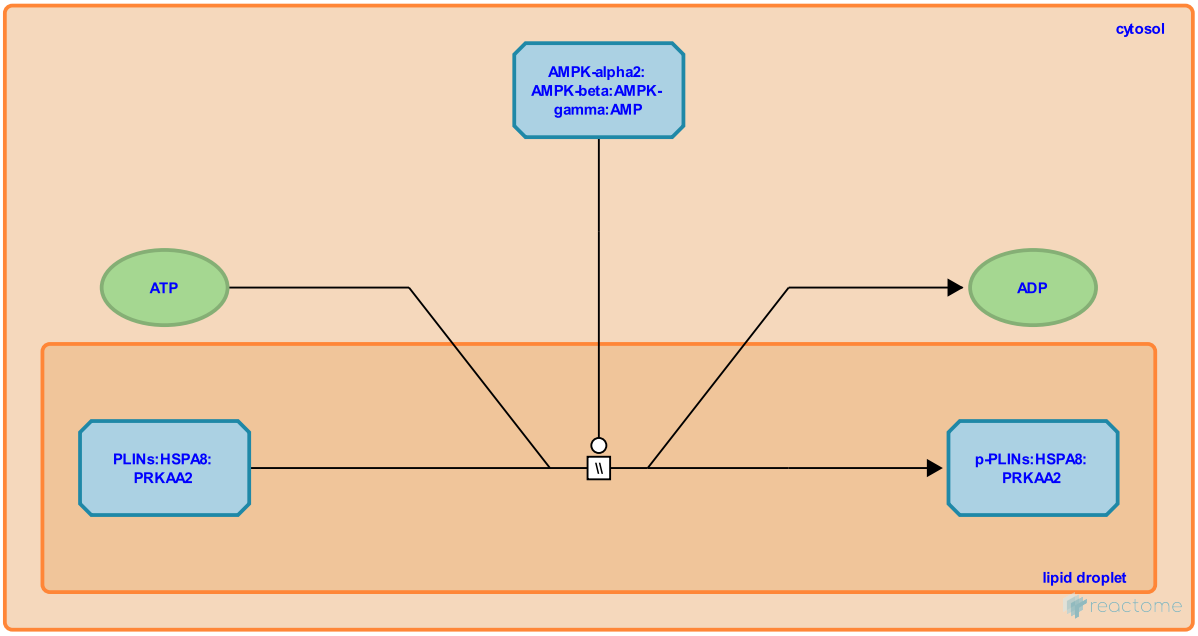
Location: Lipophagy

Stable identifier: R-HSA-9613530

Type: omitted

Compartments: lipid droplet, cytosol

Inferred from: Prkaa2 phosphorylates Plins (Mus musculus)



Lipophagy is the process of autophagic degradation of lipid droplets into fatty acids. Lipid droplets are coated with perilipin (PLIN) proteins and they need to be eliminated for the degradation of the lipids inside. Cytosolic Heat shock cognate 71 kDa protein (HSPA8) binds PLIN2 and PLIN3 on the lipid droplet surface. Subsequently, AMPK binds and phosphorylates perilipins targeting them for lipophagy (S Kaushik et al. 2015, S Kaushik et al. 2016). The precise phosphorylation site(s) on PLINs are unknown. Experiments confirming this finding were performed in mouse models.

Preceded by: PLINs:HSPA8 binds PRKAA2

Followed by: PRKAA2 dissociate from p-PLINs:HSPA8

Literature references

Cuervo, AM., Kaushik, S. (2016). AMPK-dependent phosphorylation of lipid droplet protein PLIN2 triggers its degradation by CMA. *Autophagy, 12*, 432-8. ↗

Cuervo, AM., Kaushik, S. (2015). Degradation of lipid droplet-associated proteins by chaperone-mediated autophagy facilitates lipolysis. *Nat. Cell Biol., 17*, 759-70. ↗

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PRKAA2 dissociate from p-PLINs:HSPA8 ↗

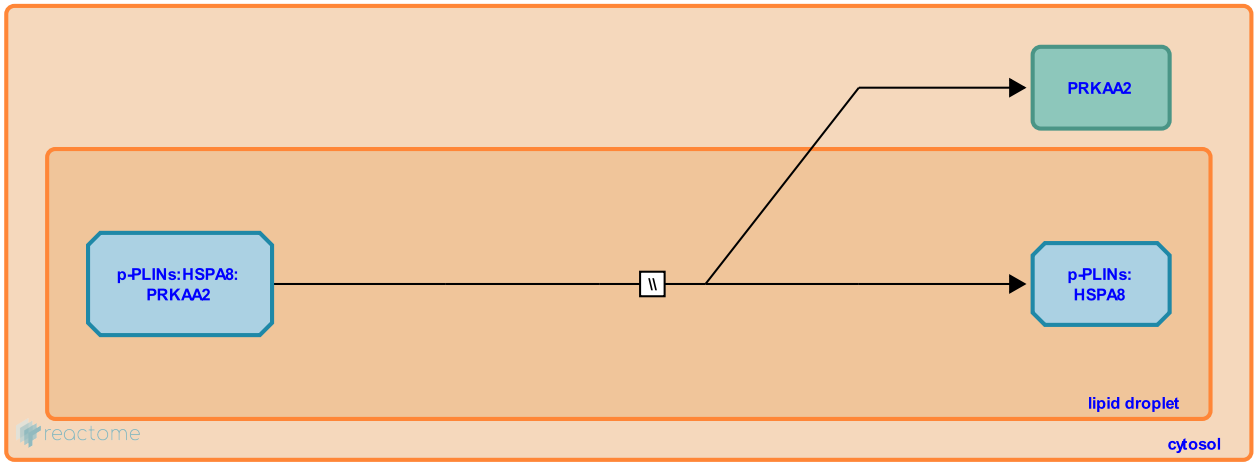
Location: Lipophagy

Stable identifier: R-HSA-9613565

Type: omitted

Compartments: lipid droplet, cytosol

Inferred from: Prkaa2 dissociate from p-Plins:Hspa8 (Mus musculus)



Once phosphorylated, PLINs are believed to dissociate from PRKAA2 and translocate to the cytosol (S Kaushik et al. 2015, S Kaushik et al. 2016). The precise dissociation mechanism of Plins is unclear. The experiments showing this finding were performed in mouse models.

Preceded by: PRKAA2 phosphorylates PLINs

Followed by: p-PLINs translocate from lipid droplet surface to cytosol, PLINs:HSPA8 binds PRKAA2

Literature references

Cuervo, AM., Kaushik, S. (2016). AMPK-dependent phosphorylation of lipid droplet protein PLIN2 triggers its degradation by CMA. *Autophagy, 12*, 432-8. ↗

Cuervo, AM., Kaushik, S. (2015). Degradation of lipid droplet-associated proteins by chaperone-mediated autophagy facilitates lipolysis. *Nat. Cell Biol., 17*, 759-70. ↗

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p-PLINs translocate from lipid droplet surface to cytosol ↗

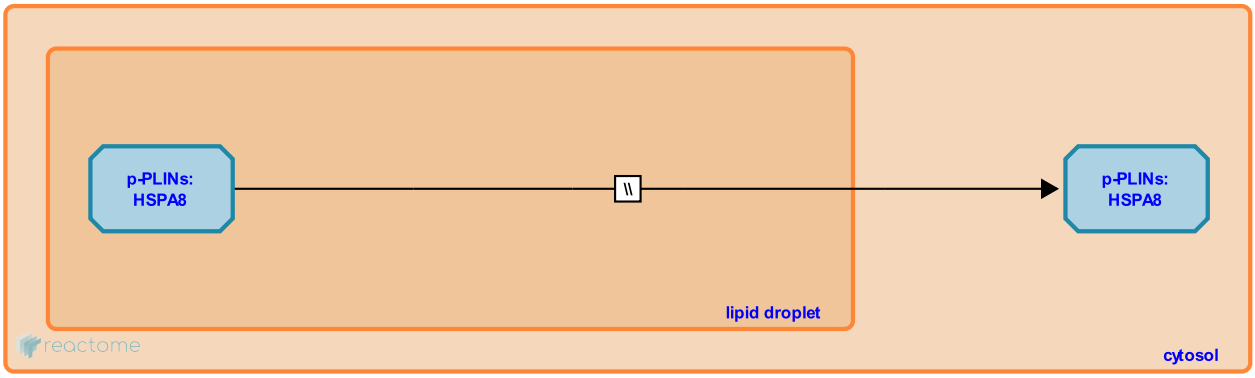
Location: Lipophagy

Stable identifier: R-HSA-9613666

Type: omitted

Compartments: lipid droplet, cytosol

Inferred from: p-Plins translocate from lipid droplet surface to cytosol (Mus musculus)



Lipophagy is the process of autophagic degradation of lipid droplets into fatty acids. Lipid droplets are coated with perilipin (PLIN) proteins and they need to be eliminated for the degradation of the lipids inside. Cytosolic Heat shock cognate 71 kDa protein (HSPA8) binds PLIN2 and PLIN3 on the lipid droplet surface. Subsequently, PRKAA2 binds and phosphorylates perilipins. Phosphorylated PLINs dissociate from PRKAA2 and are believed to translocate to the cytosol (S Kaushik et al. 2015, S Kaushik et al. 2016). Experiments suggesting this event were performed in mouse models.

Preceded by: PRKAA2 dissociate from p-PLINs:HSPA8

Literature references

Cuervo, AM., Kaushik, S. (2016). AMPK-dependent phosphorylation of lipid droplet protein PLIN2 triggers its degradation by CMA. *Autophagy, 12*, 432-8. ↗

Cuervo, AM., Kaushik, S. (2015). Degradation of lipid droplet-associated proteins by chaperone-mediated autophagy facilitates lipolysis. *Nat. Cell Biol., 17*, 759-70. ↗

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