

SESN1,2 binds L-leucine and dissociates from GATOR2

Condon, KJ., May, B., Sabatini, DM.

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

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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.

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Literature references

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Reactome database release: 88

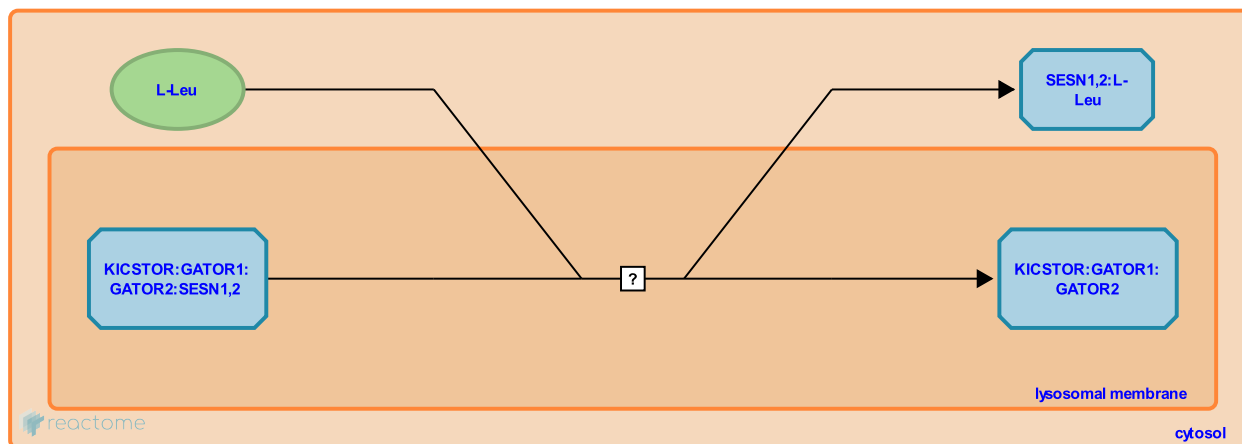
This document contains 1 reaction ([see Table of Contents](#))

SESN1,2 binds L-leucine and dissociates from GATOR2 ↗

Stable identifier: R-HSA-9639287

Type: uncertain

Compartments: lysosomal membrane



SESN2 (Sestrin2) and SESN1 (Sestrin1) each interact with the GATOR2 complex in the absence of leucine and, upon binding leucine, dissociate from the GATOR2 complex (Chantranupong et al. 2014, Parmigiani et al. 2014, Kim et al. 2015, Wolfson et al. 2016, Saxton et al. 2016). (SESN3 constitutively binds GATOR2 in the presence and absence of leucine.) When bound to GATOR2, the Sestrins appear to prevent GATOR2 from inhibiting GATOR1, a GTPase activator which negatively regulates mTORC1 activation by increasing the rate of hydrolysis of RRAGA,B:GTP to RRAGA,B:GDP. SESN1,2 complexed with GATOR2 therefore allows GATOR1 to maintain mTORC1 in the inactive state (Chantranupong et al. 2014, Parmigiani et al. 2014, Kim et al. 2015). L-leucine binds SESN1,2 and causes SESN1,2 to dissociate from GATOR2, allowing GATOR2 to inhibit GATOR1 and thereby maintain RRAGA,B in the active (GTP-bound) state (Wolfson et al. 2016, Saxton et al. 2016). GATOR1 is recruited to the lysosomal membrane by the KICSTOR complex (Wolfson et al. 2017, Peng et al. 2017).

Sestrins also appear to interact with the Rag heterodimer (Peng et al. 2014) though the interaction may be indirect (Budanov 2015).

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Editions

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