Calpain cleaves p35 to p25

Orlic-Milacic, M., Shah, K.

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. ↗

Calpain cleaves p35 to p25 ↗

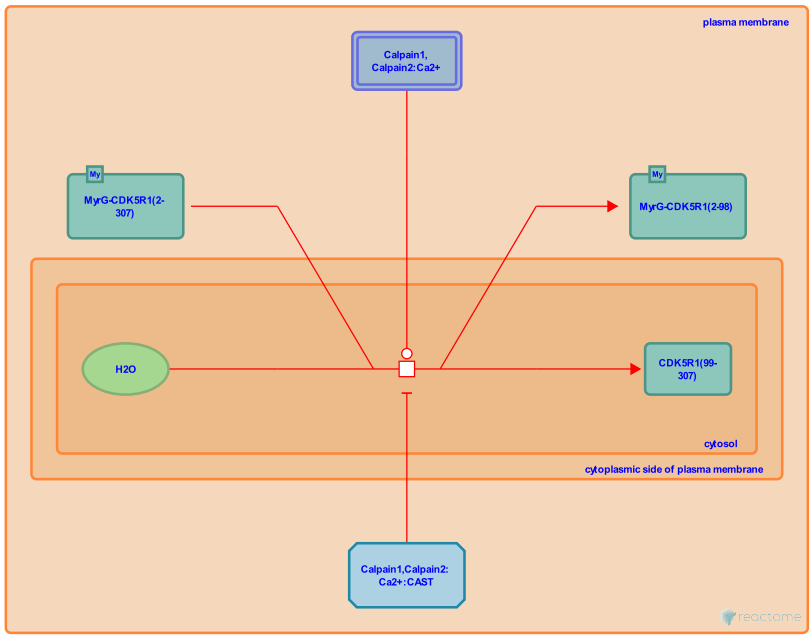
Stable identifier: R-HSA-8863012

Type: transition

Compartments: cytosol

Diseases: Alzheimer's disease

Inferred from: Calpain 1 or Calpain 2 cleaves Cdk5r1 (p35) (Mus musculus)



A variety of neurotoxic insults such as beta-amyloid (A-beta), ischemia, excitotoxicity and oxidative stress disrupt the intracellular calcium homeostasis in neurons, thereby leading to the activation of calpain, which cleaves p35 into p25 and p10 (Lee et al. 2000). p25 has a six-fold longer half-life compared to p35 and lacks the membrane anchoring signal, which results in its constitutive activation and mislocalization of the CDK5:p25 complex to the cytoplasm and the nucleus.

Calpain-mediated cleavage of p35 to p25 is inhibited by calpastatin (CAST). CAST levels are decreased in Alzheimer disease (Sato et al. 2011).

Literature references

Peng, J., Kwon, YT., Friedlander, RM., Lee, MS., Li, M., Tsai, LH. (2000). Neurotoxicity induces cleavage of p35 to p25 by calpain. *Nature, 405*, 360-4. ↗

Editions

2016-02-23	Authored	Shah, K.
2016-05-10	Edited	Orlic-Milacic, M.