HTRA1 hydrolyzes ACAN (Aggrecan)

D'Eustachio, P., Jupe, S.

12/05/2024

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. ↗
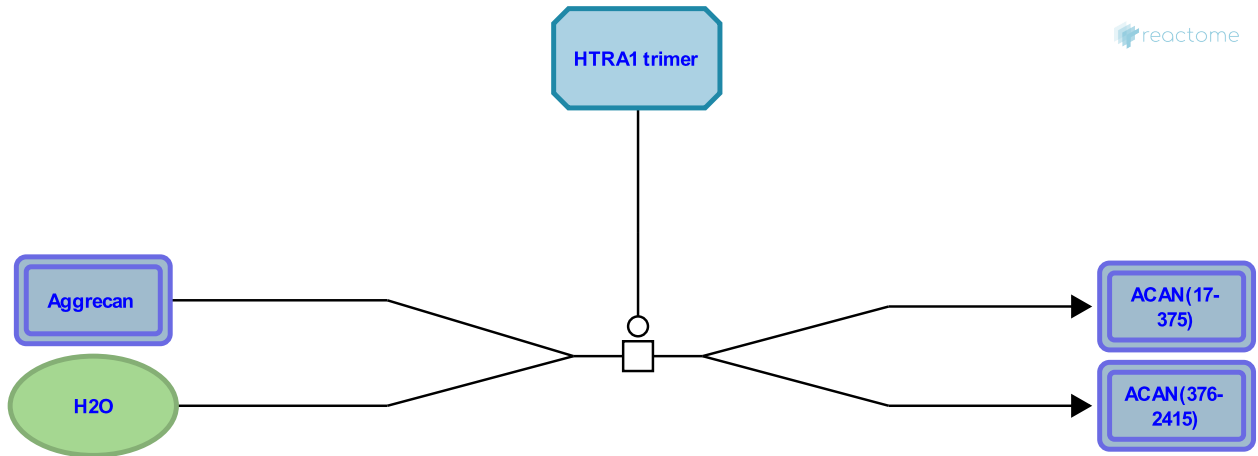
Reactome database release: 88

This document contains 1 reaction (see Table of Contents)

HTRA1 hydrolyzes ACAN (Aggrecan) ↗

Stable identifier: R-HSA-8855825

Type: transition

Compartments: extracellular region

Extracellular HTRA1 (High-temperature requirement A serine peptidase 1) catalyzes the hydrolysis of a specific peptide bond in ACAN (Aggrecan) (Chamberland et al. 2009; Hu et al. 1998). The enzyme is a homotrimer (Truebestein et al. 2011). HTRA1 is thereby implicated in the degradation of extracellular matrix. Indirect studies in mouse model systems (e.g., Oka et al. 2004) that HTRA1 may modulate the activity of Tgf-beta and thereby play additional roles, not annotated here, in the turnover of extracellular matrix both normally and during inflammation.

Literature references

Tennstaedt, A., Clausen, T., Mönig, T., Truebestein, L., Krojer, T., Kaiser, M. et al. (2011). Substrate-induced remodeling of the active site regulates human HTRA1 activity. *Nat. Struct. Mol. Biol., 18*, 386-8. ↗

Matsumoto, M., Ueta, Y., Kanda, H., Kajikawa, M., Kawaichi, M., Oka, C. et al. (2004). HtrA1 serine protease inhibits signaling mediated by Tgfbeta family proteins. *Development, 131*, 1041-53. ↗

Hu, SI., Klein, M., Nantermet, P., Carozza, M., Luk, D., Crowl, RM. (1998). Human HtrA, an evolutionarily conserved serine protease identified as a differentially expressed gene product in osteoarthritic cartilage. *J. Biol. Chem., 273*, 34406-12. ↗

Morris, EA., LaVallie, ER., Liu, L., Wang, E., Collins-Racie, LA., Jones, AR. et al. (2009). Identification of a novel HtrA1-susceptible cleavage site in human aggrecan: evidence for the involvement of HtrA1 in aggrecan proteolysis in vivo. *J. Biol. Chem., 284*, 27352-9. ↗

Editions

2016-02-06	Authored, Edited	D'Eustachio, P.
2016-02-08	Reviewed	Jupe, S.