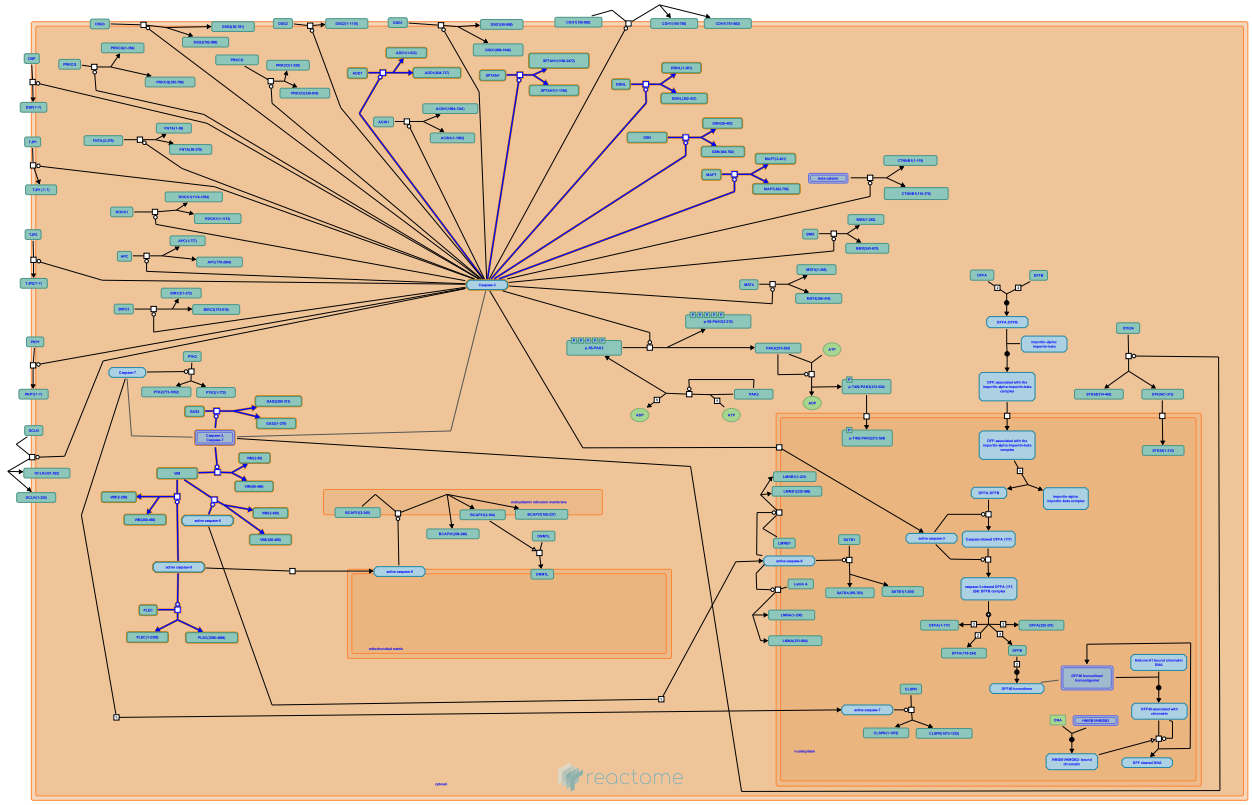
Caspase-mediated cleavage of cytoskeletal proteins



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26/01/2021

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

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. ↗

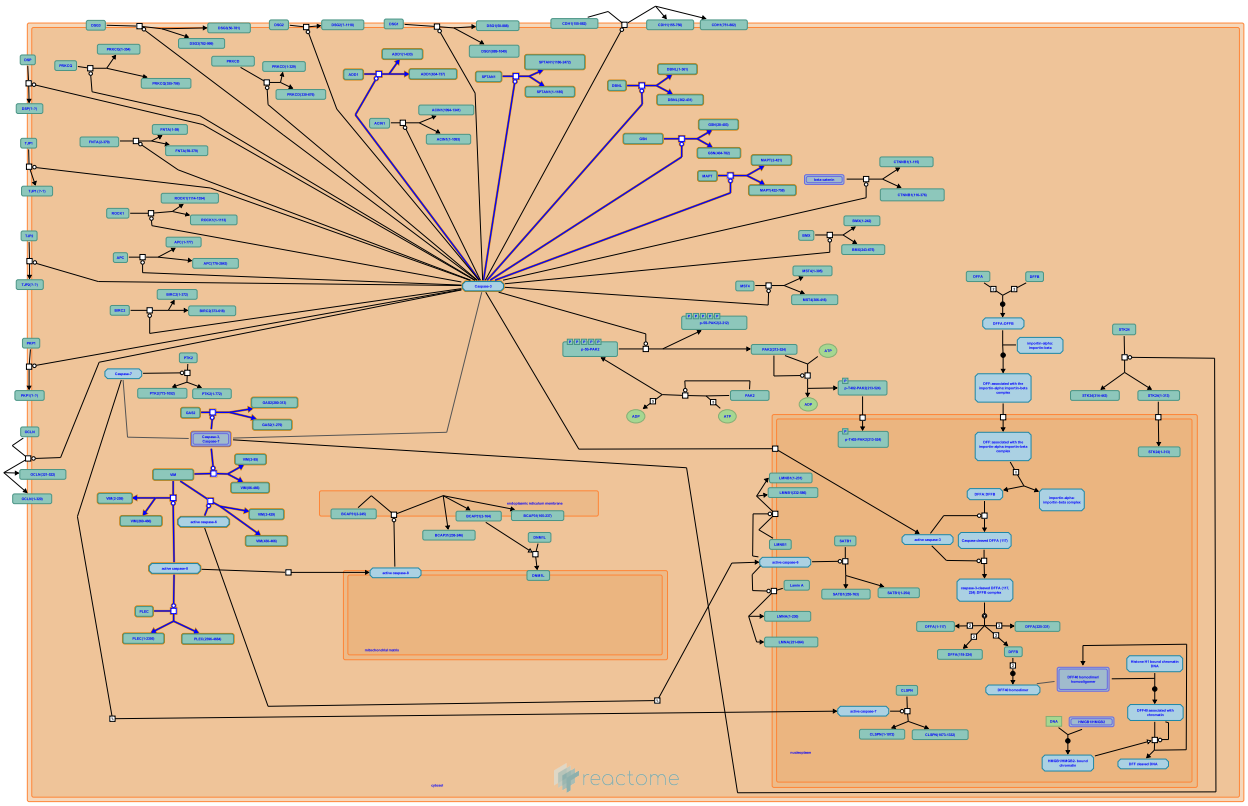
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Caspase-mediated cleavage of cytoskeletal proteins ↗

Stable identifier: R-HSA-264870



Caspase-mediated cleavage of a number of proteins in the cortical actin network ( ) microfilament system and others involved in maintenance of the cytoskeletal architecture (vimentin, or Gas2 and plectin) may directly contribute to apoptotic changes in cell shape.

Literature references

Fischer, U., Janicke, RU., Schulze-Osthoff, K. (2003). Many cuts to ruin: a comprehensive update of caspase substrates. *Cell Death Differ, 10*, 76-100. ↗

Wee, LJ., Tan, TW., Ranganathan, S. (2007). CASVM: web server for SVM-based prediction of caspase substrates cleavage sites. *Bioinformatics, 23*, 3241-3. ↗

Wee, LJ., Tan, TW., Ranganathan, S. (2006). SVM-based prediction of caspase substrate cleavage sites. *BMC Bioinformatics, 7*, S14. ↗

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2007-09-03	Authored	Schulze-Osthoff, K.
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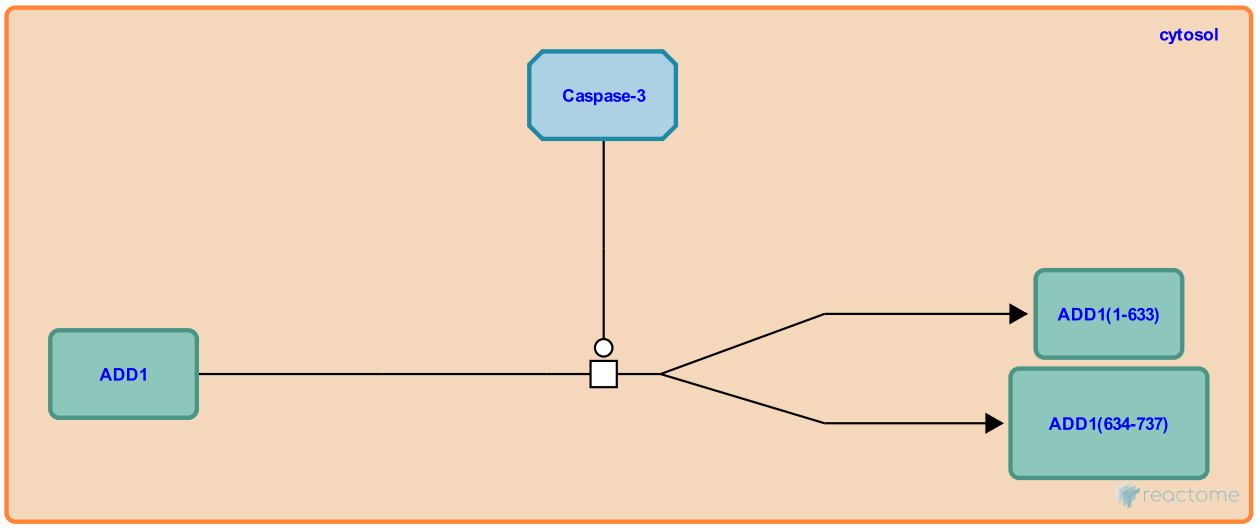
Caspase-mediated cleavage of alpha adducin ↗

Location: Caspase-mediated cleavage of cytoskeletal proteins

Stable identifier: R-HSA-201608

Type: transition

Compartments: cytosol



The cortical actin cytoskeletal network is lost during apoptosis. During apoptosis, increased phosphorylation of the actin capping protein alpha-adducin leads to its dissociation from the cytoskeleton. The caspase-3-mediated cleavage cleavage of alpha adducin at Asp-Asp-Ser-Asp(633)-Ala prevents its reassociation (van de Water et al, 2000).

Literature references

van de Water, B., Tijdens, IB., Verbrugge, A., Huigsloot, M., Dihal, AA., Stevens, JL. et al. (2000). Cleavage of the actin-capping protein alpha -adducin at Asp-Asp-Ser-Asp633-Ala by caspase-3 is preceded by its phosphorylation on serine 726 in cisplatin-induced apoptosis of renal epithelial cells. *J Biol Chem, 275*, 25805-13. ↗

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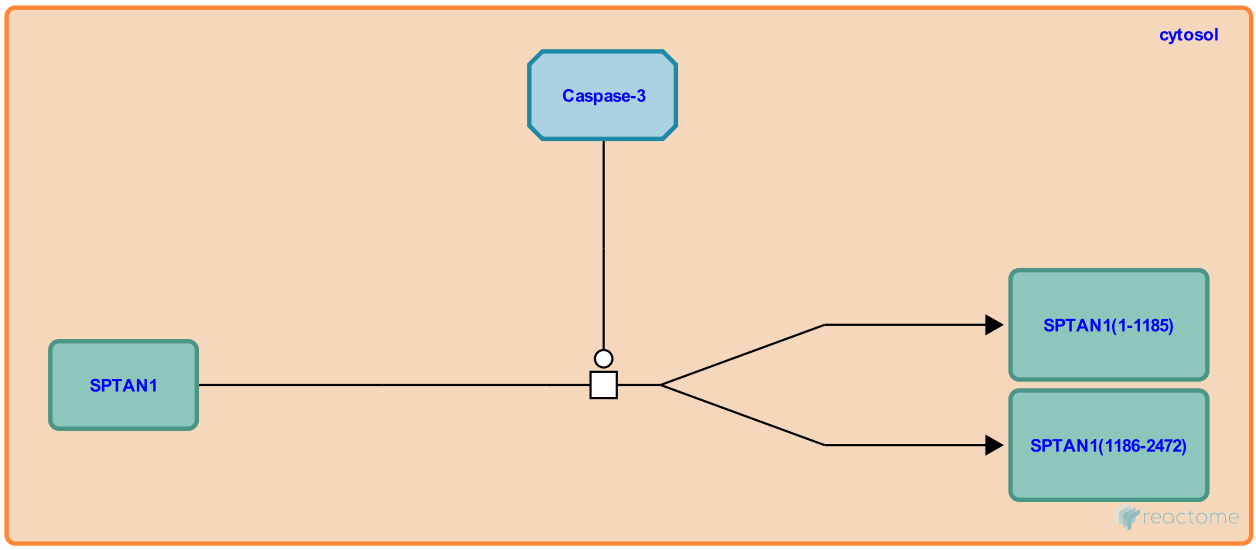
Caspase mediated cleavage of alpha-II-Fodrin ↗

Location: Caspase-mediated cleavage of cytoskeletal proteins

Stable identifier: R-HSA-202967

Type: transition

Compartments: cytosol



Apoptosis induced caspases cleave cortical actin network components including fodrin and components of the focal adhesion complex components which links membrane proteins and cortical actin filaments to the extracellular matrix (Janicke et al.,1998). Cleavage of these proteins results in disruption of the cortical cytoskeleton and may contribute to membrane blebbing (see Fischer et al., 2003). The full length 240 kDa alpha-fodrin protein can be cleaved at several sites within its sequence by activated caspases to yield amino-terminal 150 kDa, carboxy-terminal 120 kDa and 35 kDa major products. Cleavage of alpha-II fodrin leads to membrane malfunction and cell shrinkage (Janicke et al., 1998).

Literature references

Janicke, RU., Ng, P., Sprengart, ML., Porter, AG. (1998). Caspase-3 is required for alpha-fodrin cleavage but dispensable for cleavage of other death substrates in apoptosis. *J Biol Chem, 273*, 15540-5. ↗

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2007-09-03	Authored	Schulze-Osthoff, K.
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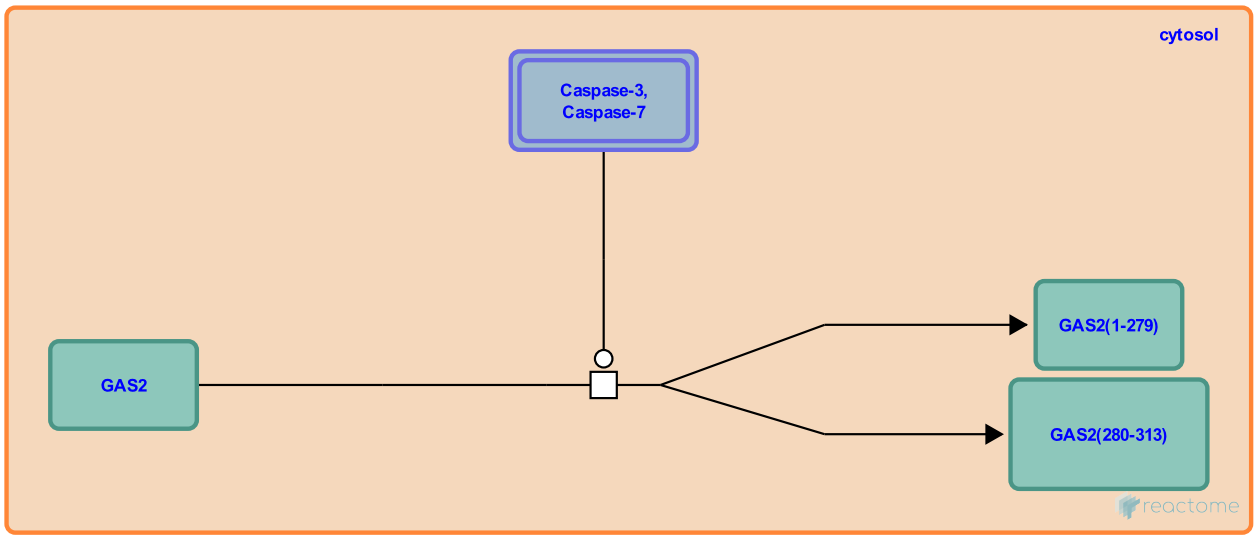
Caspase-mediated cleavage of GAS2 ↗

Location: Caspase-mediated cleavage of cytoskeletal proteins

Stable identifier: R-HSA-201639

Type: transition

Compartments: cytosol



Cleavage of Gas2 during apoptosis is associated with changes of the microfilament system but does not interfere with its ability to bind F-actin (Brancolini et al., 1995).

Literature references

Brancolini, C., Benedetti, M., Schneider, C. (1995). Microfilament reorganization during apoptosis: the role of Gas2, a possible substrate for ICE-like proteases. *EMBO J, 14*, 5179-90. ↗

Sgorbissa, A., Benetti, R., Marzinotto, S., Schneider, C., Brancolini, C. (1999). Caspase-3 and caspase-7 but not caspase-6 cleave Gas2 in vitro: implications for microfilament reorganization during apoptosis. *J Cell Sci, 112*, 4475-82. ↗

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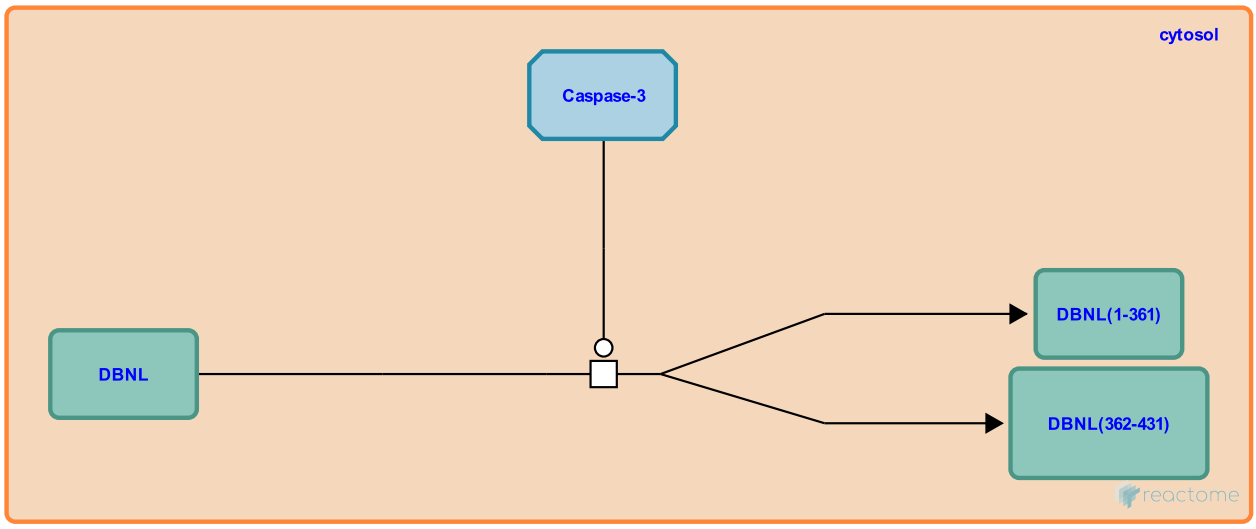
Caspase mediated cleavage of HIP-55 ↗

Location: Caspase-mediated cleavage of cytoskeletal proteins

Stable identifier: R-HSA-202966

Type: transition

Compartments: cytosol



HIP-55 is an actin binding SH3 domain protein that is cleaved by caspase-3. Cleavage results in dissociation of the actin-binding domain from the SH3 domain and may alter cell signaling to and from the actin cytoskeleton. In addition, this cleavage may be involved in the the alteration in cell morphology that occur during apoptosis (Chen et al., 2001).

Literature references

Chen, YR., Kori, R., John, B., Tan, TH. (2001). Caspase-mediated cleavage of actin-binding and SH3-domain-containing proteins cortactin, HS1, and HIP-55 during apoptosis. *Biochem Biophys Res Commun, 288*, 981-9. ↗

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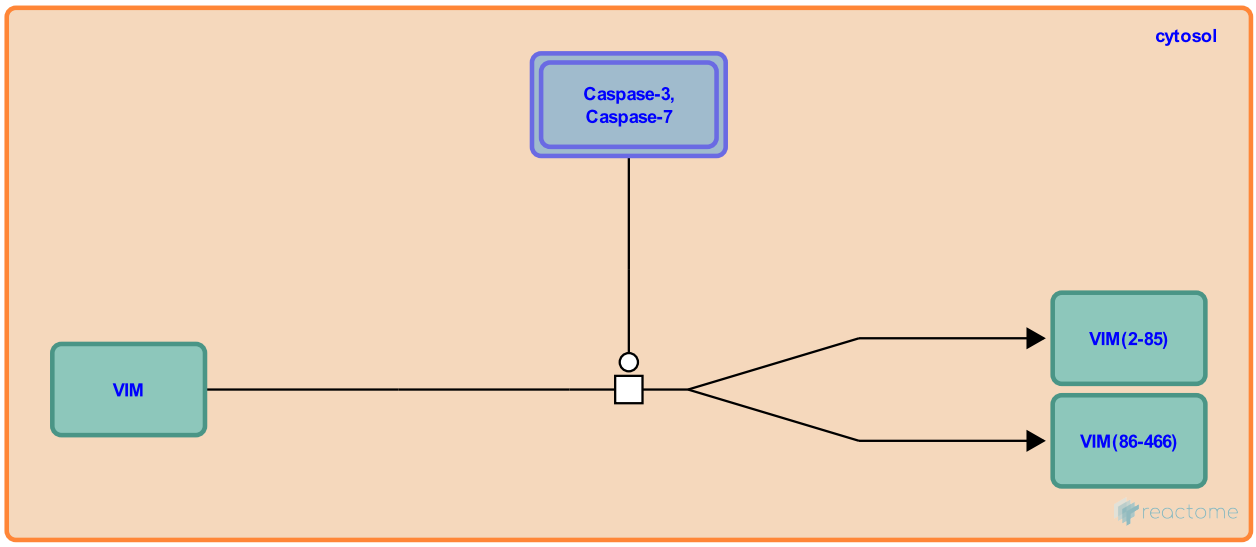
Caspase-mediated cleavage of vimentin at DSVD (85)

Location: Caspase-mediated cleavage of cytoskeletal proteins

Stable identifier: R-HSA-201628

Type: transition

Compartments: cytosol



Vimentin is cleaved by several caspases during apoptosis (Morishima et al., 1999, Byun et al., 2001). This cleavage disrupts the cytoplasmic network of intermediate filaments and coincides temporally with nuclear fragmentation. Caspase-6 recognizes and cleaves C terminal side of Asp-429. Vimentin is cleaved at Asp85 by caspases-3 and -7 (Byun et al., 2001). This clevage generates a pro-apoptotic amino-terminal cleavage product (amino acids 1-85) that amplifies the cell death signal (Byun et al., 2001).

Literature references

Byun, Y., Chen, F., Chang, R., Trivedi, M., Green, KJ., Cryns, VL. (2001). Caspase cleavage of vimentin disrupts intermediate filaments and promotes apoptosis. *Cell Death Differ, 8*, 443-50.

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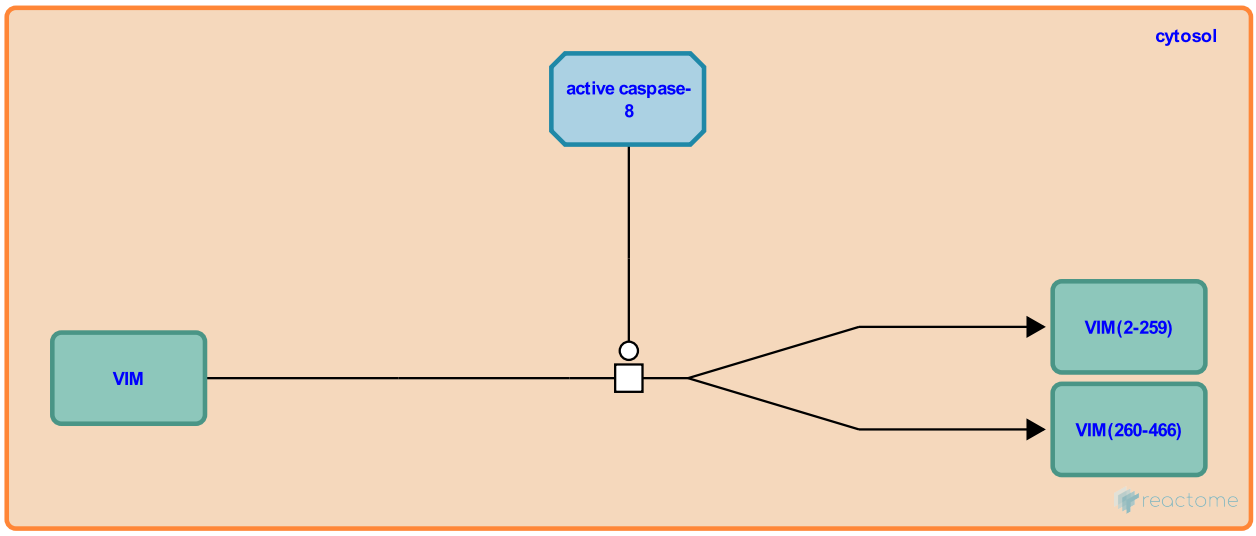
Caspase mediated cleavage of vimentin at IDVD (259) ↗

Location: Caspase-mediated cleavage of cytoskeletal proteins

Stable identifier: R-HSA-350319

Type: transition

Compartments: cytosol



Vimentin is cleaved by several caspases during apoptosis (Morishima et al., 1999, Byun et al., 2001). This clevage disrupts the cytoplasmic network of intermediate filaments and coincides temporally with nuclear fragmentation. Asp259 is recognized and cleaved by caspase-6 (Byun et al., 2001).

Literature references

Byun, Y., Chen, F., Chang, R., Trivedi, M., Green, KJ., Cryns, VL. (2001). Caspase cleavage of vimentin disrupts intermediate filaments and promotes apoptosis. *Cell Death Differ, 8*, 443-50. ↗

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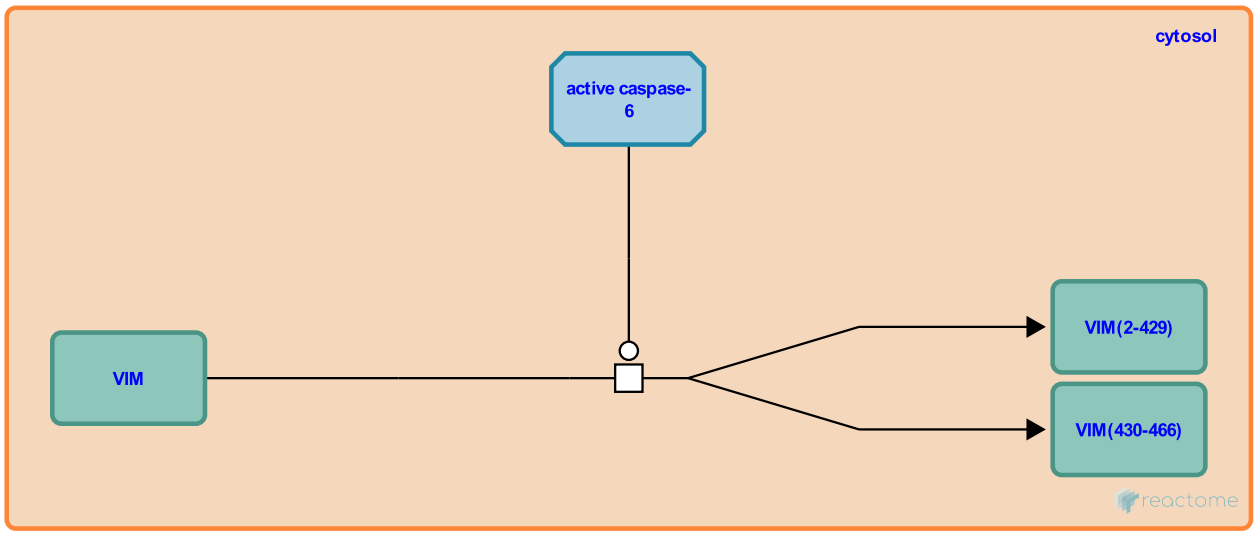
Caspase-mediated cleavage of vimentin at TNLD (429) ↗

Location: Caspase-mediated cleavage of cytoskeletal proteins

Stable identifier: R-HSA-350318

Type: transition

Compartments: cytosol



Vimentin is cleaved by several caspases during apoptosis (Morishima et al., 1999, Byun et al., 2001). This clevage disrupts the cytoplasmic network of intermediate filaments and coincides temporally with nuclear fragmentation. Caspase-6 recognizes and cleaves C terminal side of Asp-429.

Literature references

Morishima, N. (1999). Changes in nuclear morphology during apoptosis correlate with vimentin cleavage by different caspases located either upstream or downstream of Bcl-2 action. *Genes Cells, 4*, 401-14. ↗

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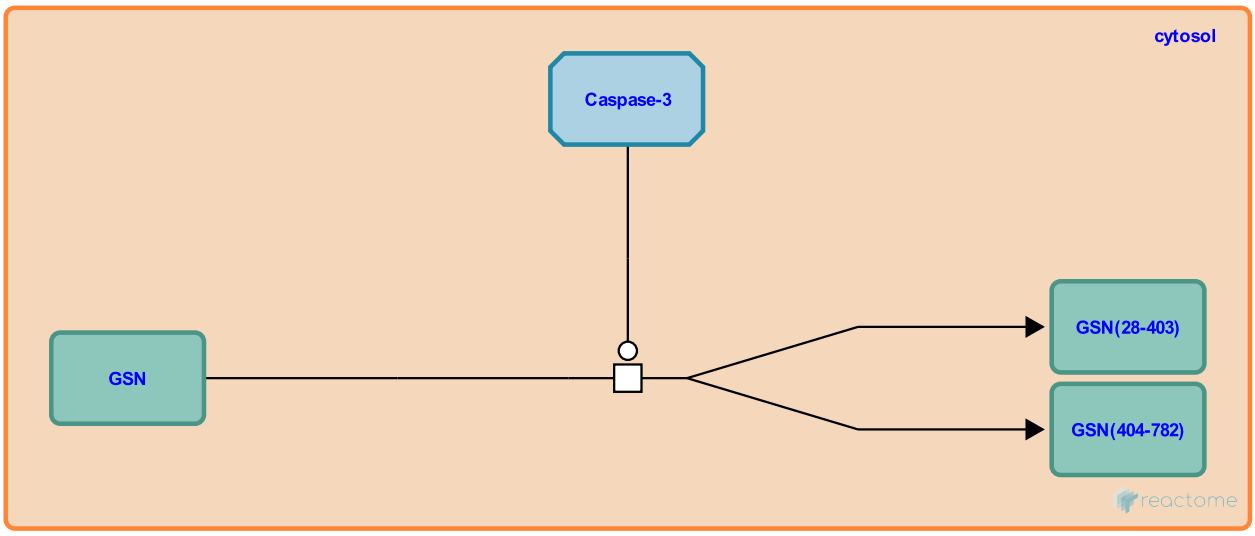
Caspase-mediated cleavage of gelsolin ↗

Location: Caspase-mediated cleavage of cytoskeletal proteins

Stable identifier: R-HSA-201622

Type: transition

Compartments: cytosol



Gelsolin is cleaved by caspase-3 generating a constitutively

active fragment that can depolymerize F-actin contributing to actin cytoskeletal collapse (Kothakota et al., 1997)

Literature references

Kothakota, S., Azuma, T., Reinhard, C., Klippel, A., Tang, J., Chu, K. et al. (1997). Caspase-3-generated fragment of gelsolin: effector of morphological change in apoptosis. *Science, 278*, 294-8. ↗

Geng, YJ., Azuma, T., Tang, JX., Hartwig, JH., Muszynski, M., Wu, Q. et al. (1998). Caspase-3-induced gelsolin fragmentation contributes to actin cytoskeletal collapse, nucleolysis, and apoptosis of vascular smooth muscle cells exposed to proinflammatory cytokines. *Eur J Cell Biol, 77*, 294-302. ↗

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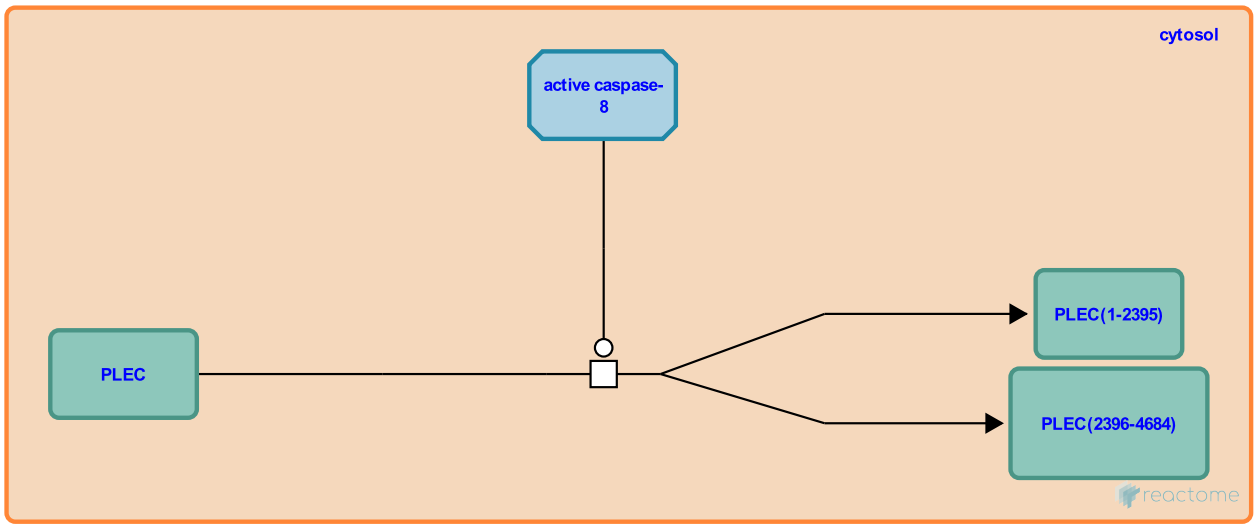
Caspase-mediated cleavage of plectin-1 ↗

Location: Caspase-mediated cleavage of cytoskeletal proteins

Stable identifier: R-HSA-201637

Type: transition

Compartments: cytosol



Plectin is a major cross-linking protein of the three main cytoplasmic filament systems. Caspase-8 mediated cleavage of plectin 1 appears to contribute to disruption of the microfilament system during the early stages of apoptosis (Stegh et al., 2000).

Literature references

Stegh, AH., Herrmann, H., Lampel, S., Weisenberger, D., Andrä, K., Seper, M. et al. (2000). Identification of the cytolinker plectin as a major early in vivo substrate for caspase 8 during CD95- and tumor necrosis factor receptor-mediated apoptosis. *Mol Cell Biol, 20*, 5665-79. ↗

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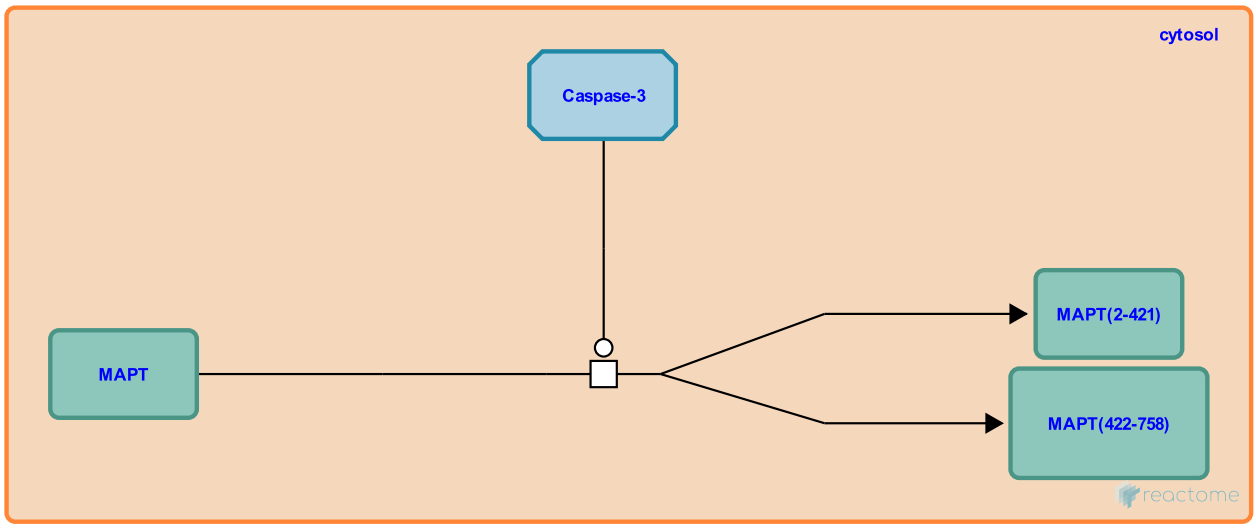
Caspase-mediated cleavage of Tau ↗

Location: Caspase-mediated cleavage of cytoskeletal proteins

Stable identifier: R-HSA-201629

Type: transition

Compartments: cytosol



Caspase-3 cleaves Tau at position 421 in vitro producing an N-terminal fragment that functions as an apoptotic effector (Fasulo et al., 2000).

Literature references

Fasulo, L., Ugolini, G., Visintin, M., Bradbury, A., Brancolini, C., Verzillo, V. et al. (2000). The neuronal microtubule-associated protein tau is a substrate for caspase-3 and an effector of apoptosis. *J Neurochem, 75*, 624-33. ↗

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