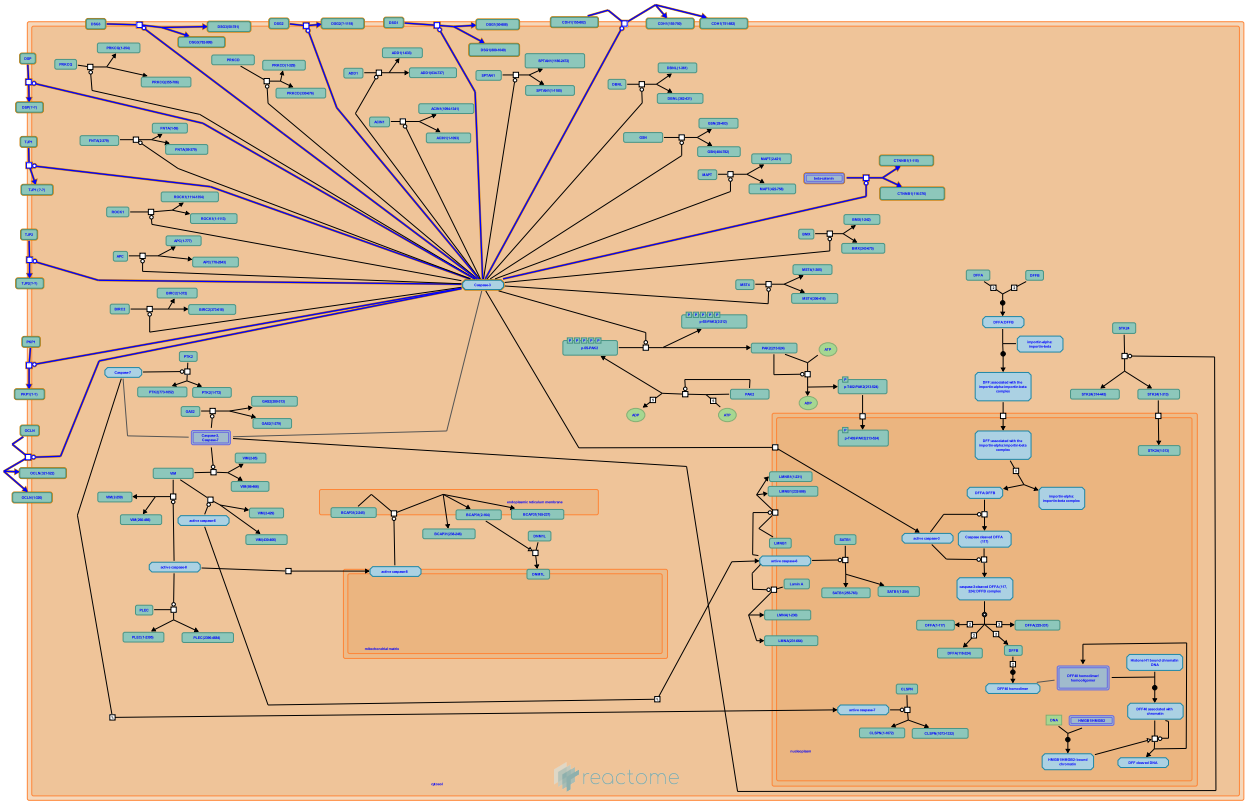
Apoptotic cleavage of cell adhesion pro-teins



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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

07/05/2024

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. ↗

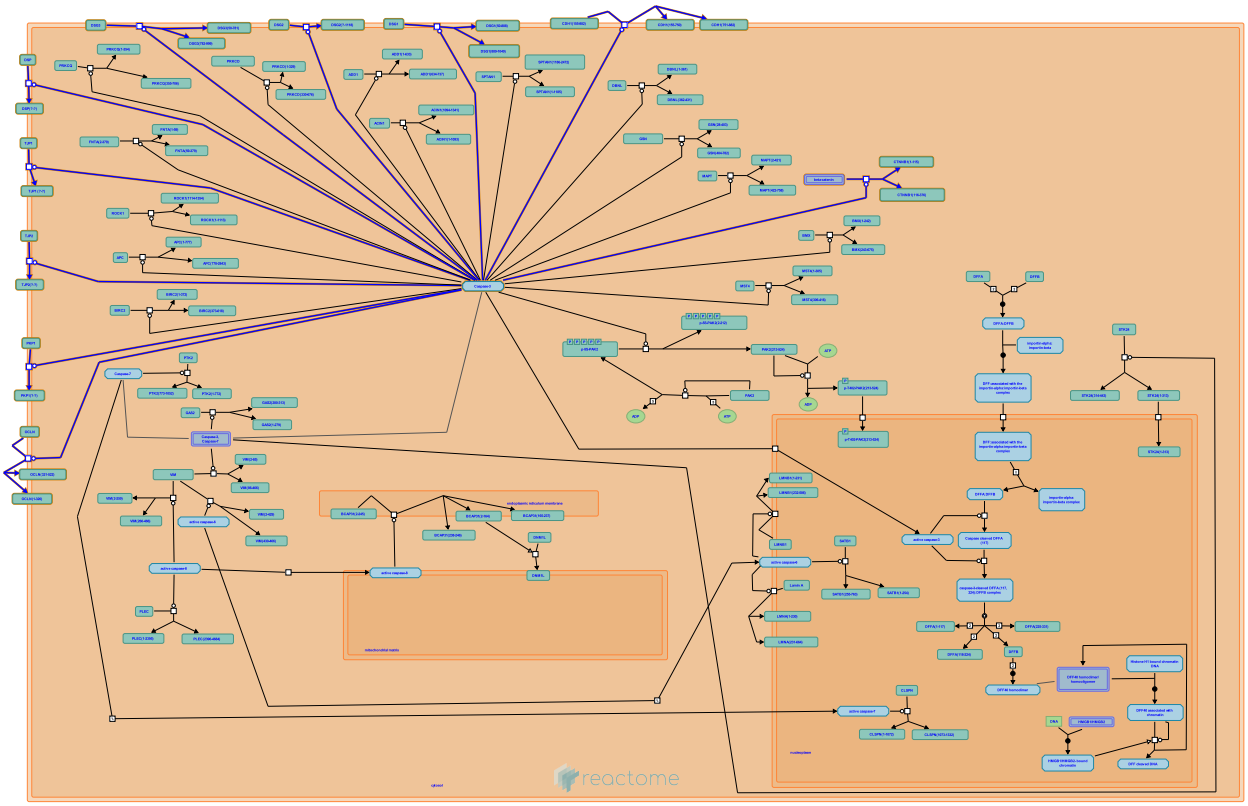
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Apoptotic cleavage of cell adhesion proteins ↗

Stable identifier: R-HSA-351906



Apoptotic cells show dramatic rearrangements of tight junctions, adherens junctions, and desmosomes (Abreu et al., 2000). Desmosome-specific members of the cadherin superfamily of cell adhesion molecules including desmoglein-3, plakophilin-1 and desmoplakin are cleaved by caspases after onset of apoptosis (Weiske et al., 2001). Cleavage results in the disruption of the desmosome structure and thus contributes to cell rounding and disintegration of the intermediate filament system (Weiske et al., 2001).

Literature references

Weiske, J., Tauber, R., Schroder, W., Hatzfeld, M., Schoneberg, T., Huber, O. (2001). The fate of desmosomal proteins in apoptotic cells. *J Biol Chem, 276*, 41175-81. ↗

La Gatta, A., Lanza, A., Gombos, F., Cammarota, M., De Rosa, A., Cirillo, N. et al. (2008). The most widespread desmosomal cadherin, desmoglein 2, is a novel target of caspase 3-mediated apoptotic machinery. *J Cell Biochem, 103*, 598-606. ↗

Green, KJ., Getsios, S., Dusek, RL., Cryns, VL., Chen, F., Amargo, EV. et al. (2006). The differentiation-dependent desmosomal cadherin desmoglein 1 is a novel caspase-3 target that regulates apoptosis in keratinocytes. *J Biol Chem, 281*, 3614-24. ↗

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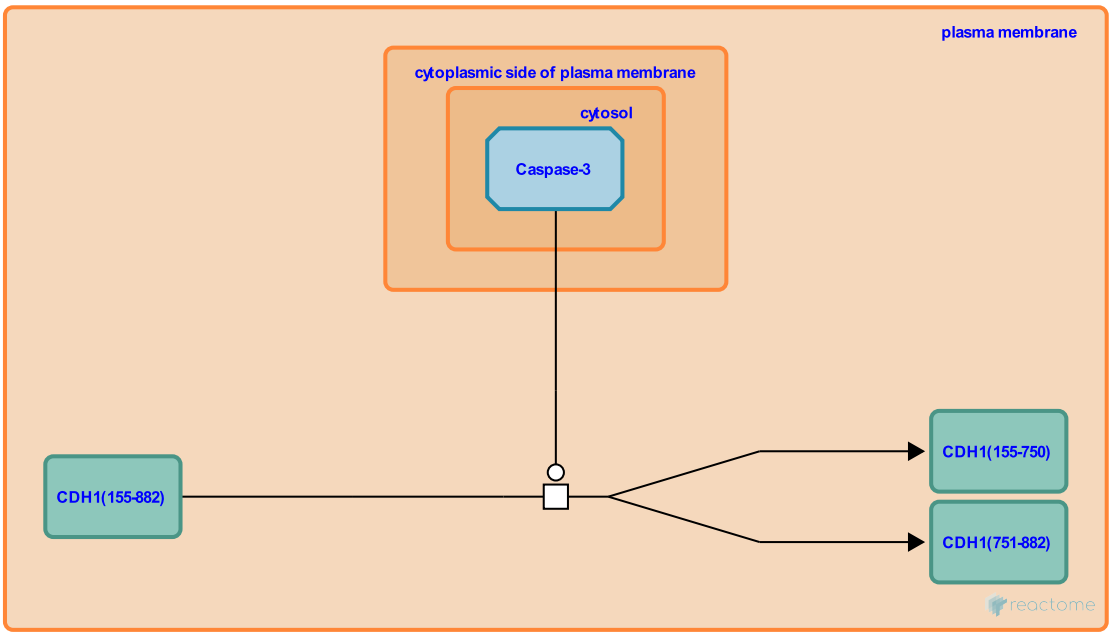
Caspase-mediated cleavage of E-Cadherin ↗

Location: Apoptotic cleavage of cell adhesion proteins

Stable identifier: R-HSA-202939

Type: transition

Compartments: plasma membrane



The cleavage of E-cadherin at both the intracellular and extracellular domains likely contributes to the disruption of cadherin-mediated cell-cell contacts in apoptotic cells. Loss of cell contact is necessary for cell rounding and exit from the epithelium (Steinhusen et al., 2001).

Literature references

Huber, O., Bommert, K., Steinhusen, U., Badock, V., Tauber, R., Weiske, J. (2001). Cleavage and shedding of E-cadherin after induction of apoptosis. *J. Biol. Chem., 276*, 4972-80. ↗

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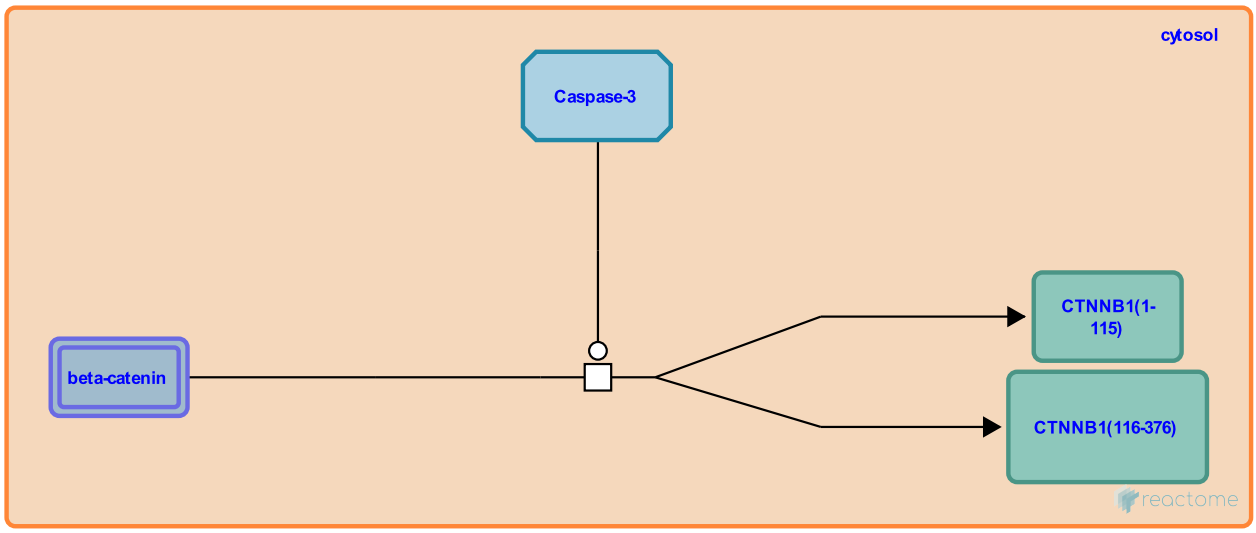
Caspase mediated cleavage of beta-catenin ↗

Location: Apoptotic cleavage of cell adhesion proteins

Stable identifier: R-HSA-202969

Type: transition

Compartments: cytosol



Apoptosis-induced cleavage of beta-catenin by caspase 3 results in reduced alpha catenin binding, relocalization to the cytoplasm and a reduction in cell-cell contact. In addition, the resulting proteolytic fragments have reduced transcription factor activity (Steinhusen et al., 2000).

Literature references

Bommert, K., Bauer, A., Steinhusen, U., Behrens, J., Wittman-Liebold, B., Badock, V. et al. (2000). Apoptosis-induced cleavage of beta-catenin by caspase-3 results in proteolytic fragments with reduced transactivation potential. *J Biol Chem, 275*, 16345-53. ↗

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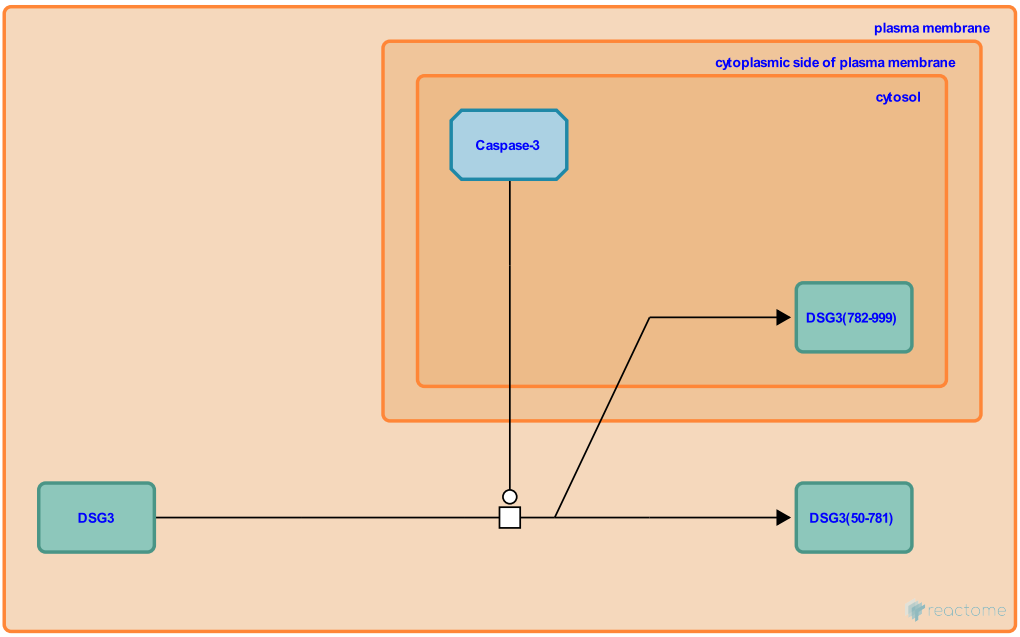
Caspase-mediated cleavage of Desmoglein 3

Location: Apoptotic cleavage of cell adhesion proteins

Stable identifier: R-HSA-201631

Type: transition

Compartments: plasma membrane, cytosol



In epithelial cells, desmosomes are anchoring junctions that mediate strong cell-cell contacts. Desmosomal proteins are proteolytically targeted during apoptosis (Weiske et al., 2001). Desmogleins are a major component of the desmosome are specifically cleaved after onset of apoptosis. Cleavage of desmosomal proteins results in the disruption of the structure of desmosomes and contributes to cell rounding and disassembly of the intermediate filament network (Weiske et al., 2001). The cytosolic fragment has implications for the autoimmune disease, Pemphigus vulgaris (Tong et al. 2006).

Literature references

Weiske, J., Tauber, R., Schroder, W., Hatzfeld, M., Schoneberg, T., Huber, O. (2001). The fate of desmosomal proteins in apoptotic cells. *J Biol Chem, 276*, 41175-81.

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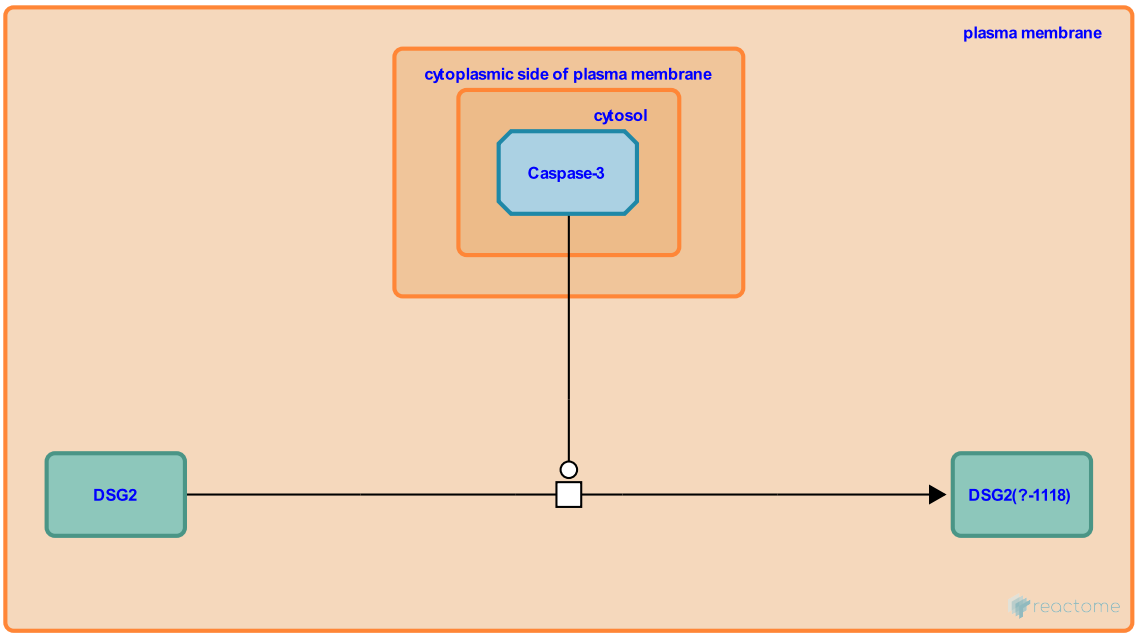
Caspase-mediated cleavage of Desmoglein 2 ↗

Location: Apoptotic cleavage of cell adhesion proteins

Stable identifier: R-HSA-351877

Type: transition

Compartments: plasma membrane



In apoptotic cells, intercellular contacts are disrupted through the activity of caspases. Apoptotic cleavage of Dsg2,the most widespread desmosomal cadherin, is mediated by caspase 3 in epithelial cells (Cirillo et al., 2008).

Literature references

La Gatta, A., Lanza, A., Gombos, F., Cammarota, M., De Rosa, A., Cirillo, N. et al. (2008). The most widespread desmosomal cadherin, desmoglein 2, is a novel target of caspase 3-mediated apoptotic machinery. *J Cell Biochem, 103*, 598-606. ↗

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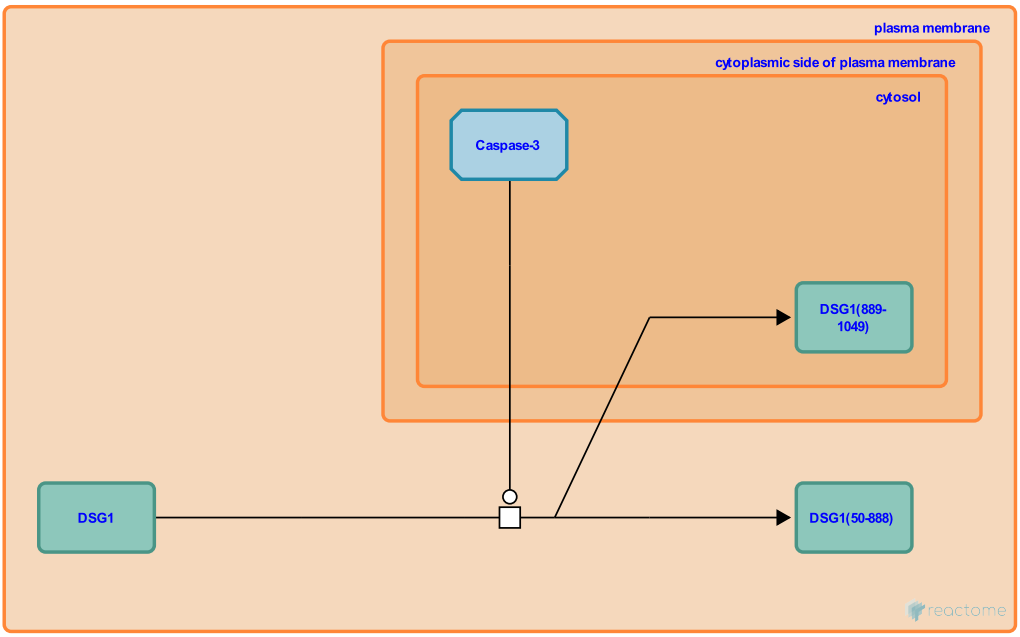
Caspase-mediated cleavage of Desmoglein 1 ↗

Location: Apoptotic cleavage of cell adhesion proteins

Stable identifier: R-HSA-202917

Type: transition

Compartments: plasma membrane, cytosol



Caspase mediated cleavage of desmoglein 1 leads to decreased expression at the cell surface and re-localization of its C terminus diffusely throughout the cytoplasm. Cleavage is thought to contribute to the dismantling of desmosomes during keratinocyte apoptosis (Dusek et al., 2006).

Literature references

Green, KJ., Getsios, S., Dusek, RL., Cryns, VL., Chen, F., Amargo, EV. et al. (2006). The differentiation-dependent desmosomal cadherin desmoglein 1 is a novel caspase-3 target that regulates apoptosis in keratinocytes. *J Biol Chem, 281*, 3614-24. ↗

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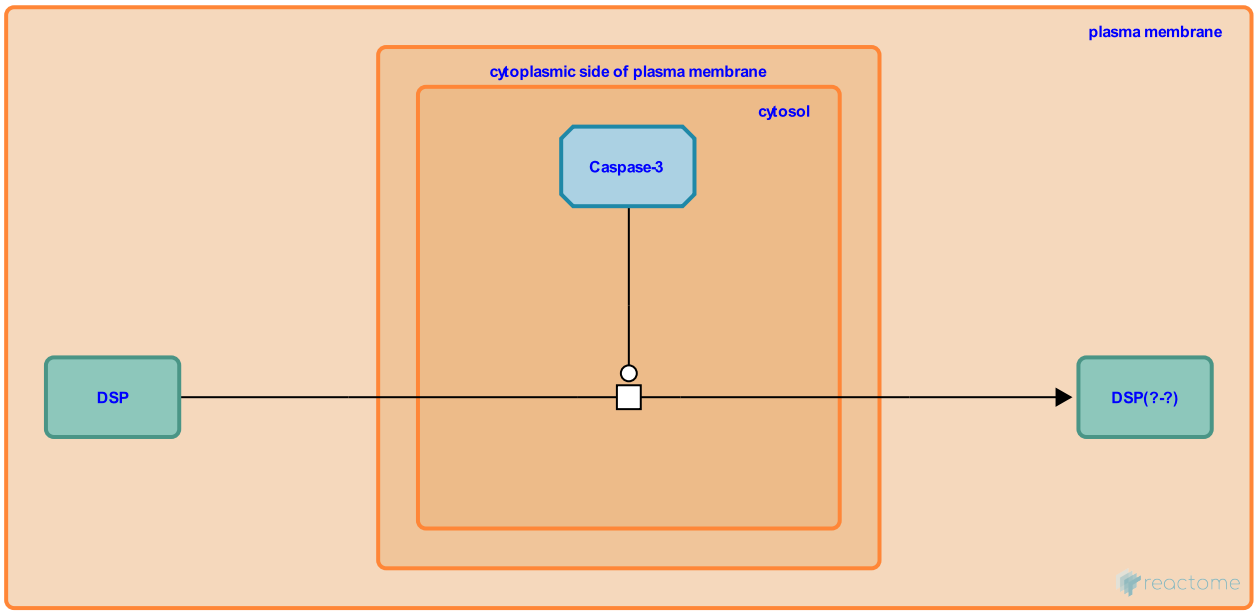
Caspase-mediated cleavage of Desmoplakin ↗

Location: Apoptotic cleavage of cell adhesion proteins

Stable identifier: R-HSA-201636

Type: transition

Compartments: cytosol



Cleavage of desmosomal proteins including desmoplakin contributes to cell rounding and disintegration of the intermediate filament system (Weiske et al., 2001). Caspase-3 inhibition prevents desmoplakin cleavage, implicating caspase-3 as the responsible endopeptidase (Weiske et al. 2001).

Literature references

Weiske, J., Tauber, R., Schroder, W., Hatzfeld, M., Schoneberg, T., Huber, O. (2001). The fate of desmosomal proteins in apoptotic cells. *J Biol Chem, 276*, 41175-81. ↗

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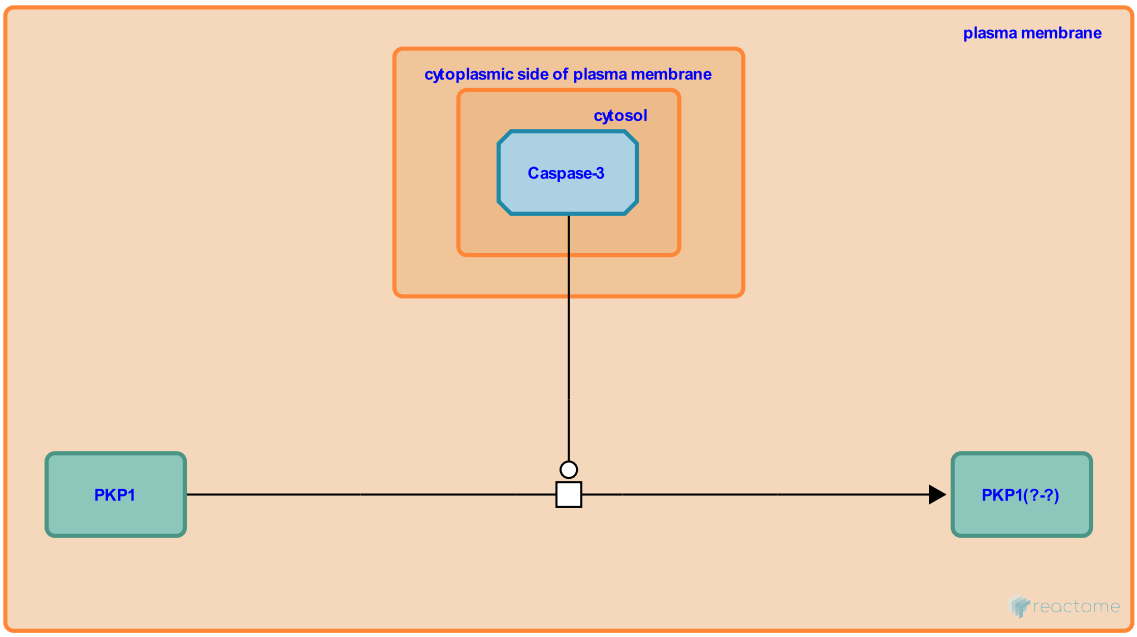
Caspase-mediated cleavage of plakophilin-1 ↗

Location: Apoptotic cleavage of cell adhesion proteins

Stable identifier: R-HSA-201595

Type: transition

Compartments: plasma membrane



Desmosomes represent one of the anchoring junctions mediating strong cell-cell contacts.Desmosomal plaque proteins including the head domain of plakophilin provide interaction sites for cytokeratin filaments (see references in Weiske et al.,2001). Proteolytic fragmentation of these proteins prevents binding of intermediate filaments and in consequence results in remodeling of the intermediate filament cytoskeleton (Weiske et al., 2001).Cleaved Plakophilin-1 appears to be impaired in supporting the formation and maintenance of desmosomes during apoptosis (Weiske et al., 2001). Caspase-3 inhibition prevents cleavage of Plakophilin-1, implicating Caspase-3 as the responsible endopeptidase (Weiske et al. 2001).

Literature references

Weiske, J., Tauber, R., Schroder, W., Hatzfeld, M., Schoneberg, T., Huber, O. (2001). The fate of desmosomal proteins in apoptotic cells. *J Biol Chem, 276*, 41175-81. ↗

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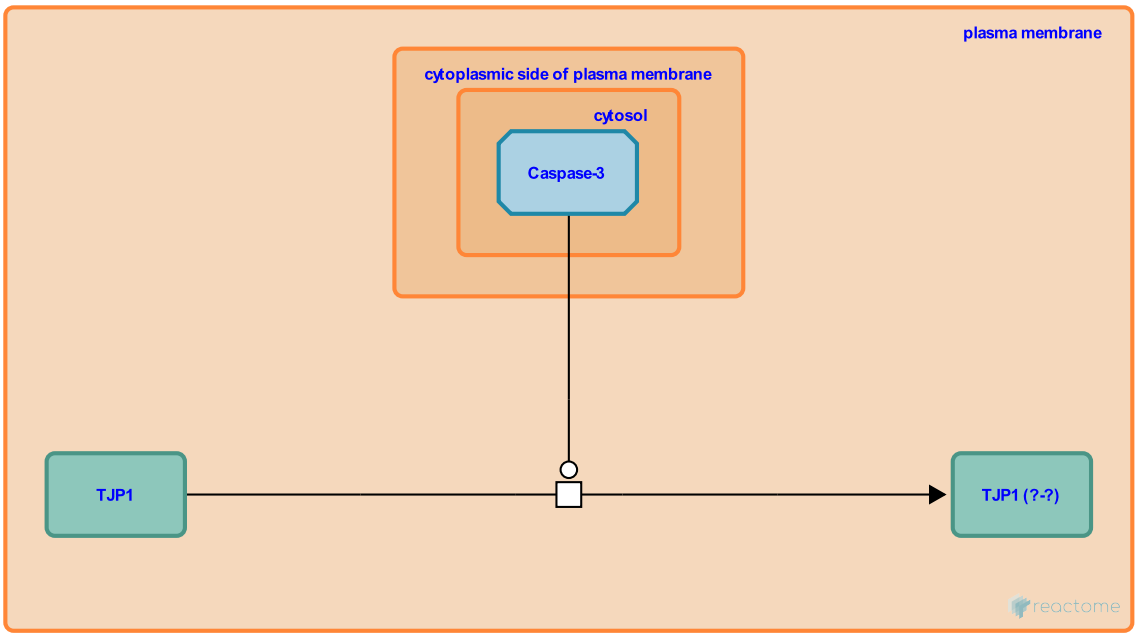
Caspase-mediated cleavage of TJP1 ↗

Location: Apoptotic cleavage of cell adhesion proteins

Stable identifier: R-HSA-351913

Type: transition

Compartments: plasma membrane



Cleavage of the C-terminal cytoplasmic domain of occludin during apoptosis generates a fragment that can no longer associate with the cytoplasmic adapter proteins ZO-1, -2 and -3 and, as a consequence, with the actin cytoskeleton (Bojarski et al., 2003). Cleavage of ZO-1 and ZO-2 further disrupts tight junction structure and function. Notably, claudins, which are associated with ZO-1, ZO-2 and ZO-3, completely lose their linkage to the actin cytoskeleton and other ZO-1-, ZO-2-, ZO-3-interacting proteins (Bojarski et al., 2003). Caspase-3 was found to be responsible for TJP1 (ZO-1) cleavage in both dog and mouse cells (Chin et al. 2006, Zehendner et al. 2011).

Literature references

Fromm, M., Mankertz, J., Weiske, J., Florian, P., Tauber, R., Schulzke, JD. et al. (2004). The specific fates of tight junction proteins in apoptotic epithelial cells. *J Cell Sci, 117*, 2097-107. ↗

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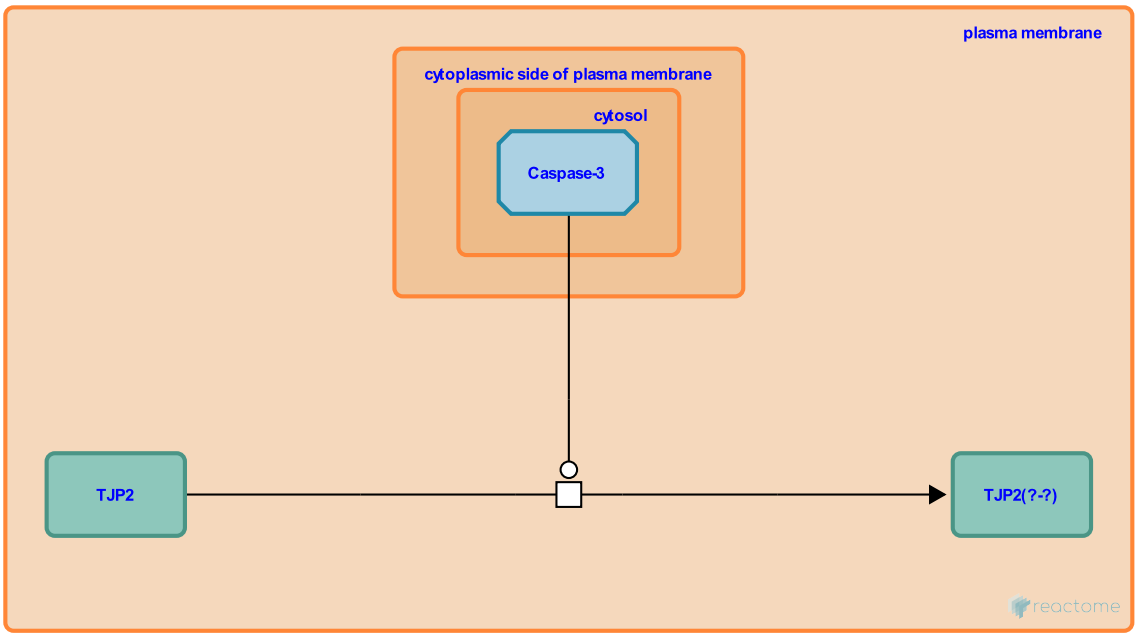
Caspase-mediated cleavage of ZO-2 ↗

Location: Apoptotic cleavage of cell adhesion proteins

Stable identifier: R-HSA-351871

Type: transition

Compartments: plasma membrane



Cleavage of the C-terminal cytoplasmic domain of occludin during apoptosis generates a fragment that can no longer associate with the cytoplasmic adapter proteins ZO-1, -2 and -3 and, as a consequence, with the actin cytoskeleton (Bojarski et al., 2003). Cleavage of ZO-1 and ZO-2 further disrupts tight junction structure and function. Notably, claudins, which are associated with ZO-1, ZO-2 and ZO-3, completely lose their linkage to the actin cytoskeleton and other ZO-1-, ZO-2-, ZO-3-interacting proteins (Bojarski et al., 2003). Inhibition of caspase-3 prevents cleavage of ZO-2, implicating caspase-3 as the responsible endopeptidase (Bojarski et al. 2004).

Literature references

Fromm, M., Mankertz, J., Weiske, J., Florian, P., Tauber, R., Schulzke, JD. et al. (2004). The specific fates of tight junction proteins in apoptotic epithelial cells. *J Cell Sci, 117*, 2097-107. ↗

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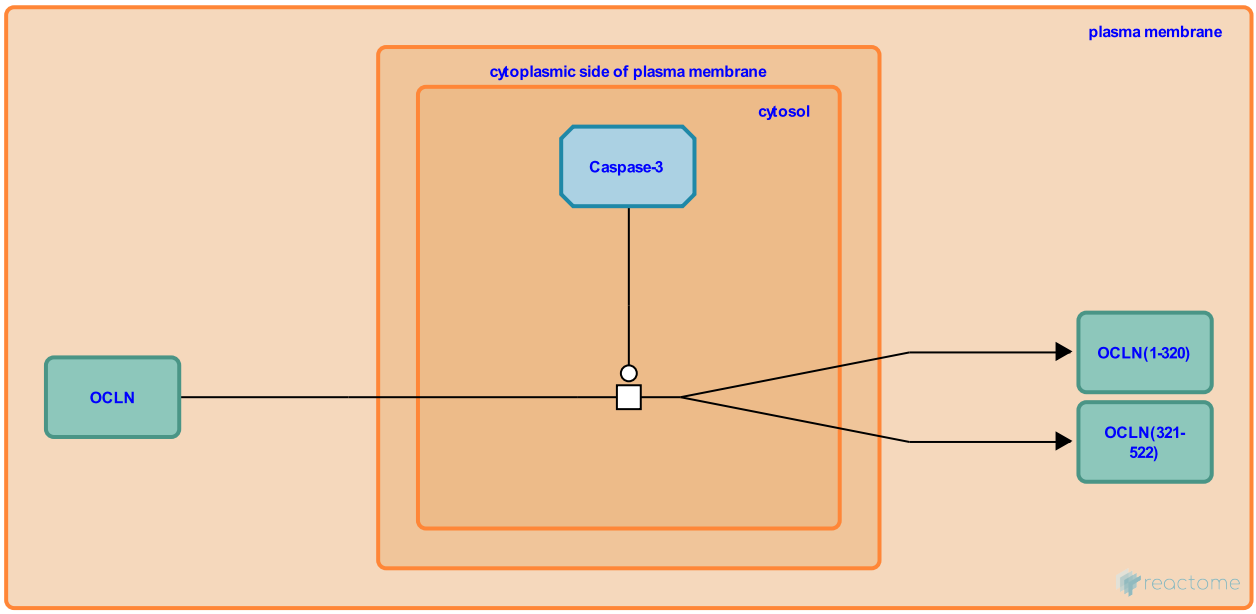
Caspase-mediated cleavage of occludin ↗

Location: Apoptotic cleavage of cell adhesion proteins

Stable identifier: R-HSA-351876

Type: transition

Compartments: cytosol



Following iinduction of apoptosis in epithelial cells, tight junction are disrupted. Tight junction proteins, including the the transmembrane protein occludin and the cytoplasmic adaptor proteins ZO-1 and ZO-2 are fragmented by caspase cleavage (Bojarski et al., 2004). Inhibition of caspase-3 prevents cleavage of occludin, implicating caspase-3 as the responsible endopeptidase (Bojarski et al. 2004).

Literature references

Fromm, M., Mankertz, J., Weiske, J., Florian, P., Tauber, R., Schulzke, JD. et al. (2004). The specific fates of tight junction proteins in apoptotic epithelial cells. *J Cell Sci, 117*, 2097-107. ↗

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Table of Contents