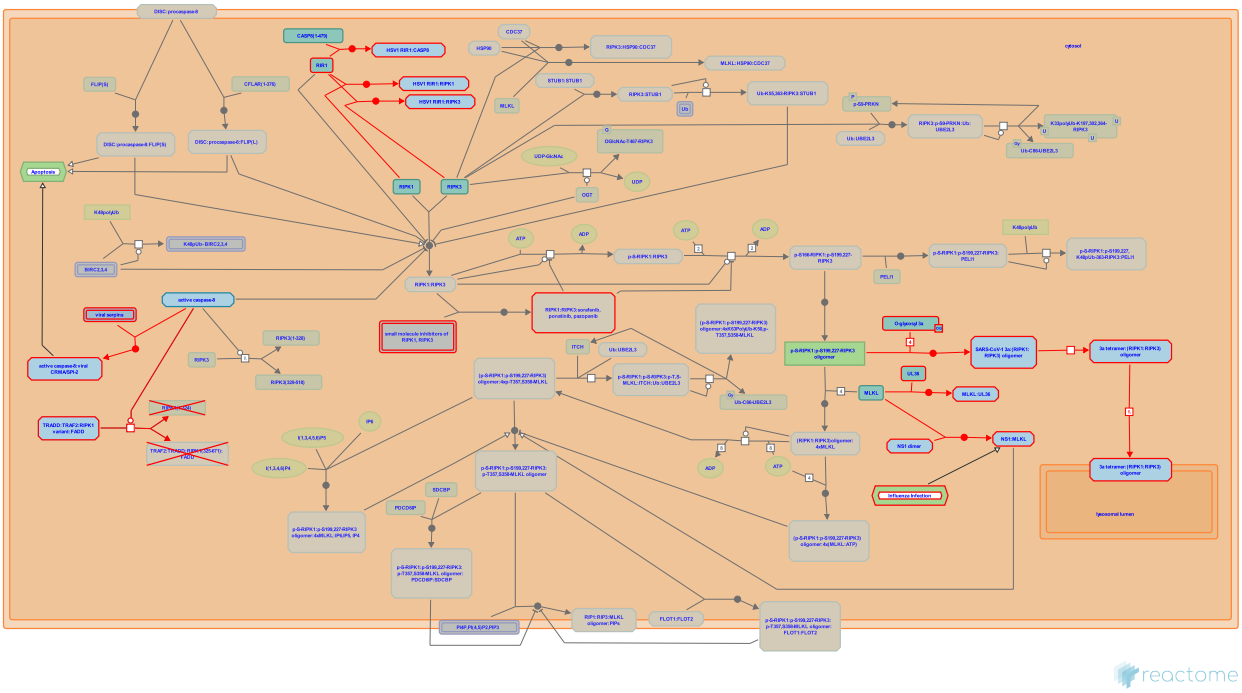
Defective RIPK1-mediated regulated necrosis



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26/04/2024

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.

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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. ↗

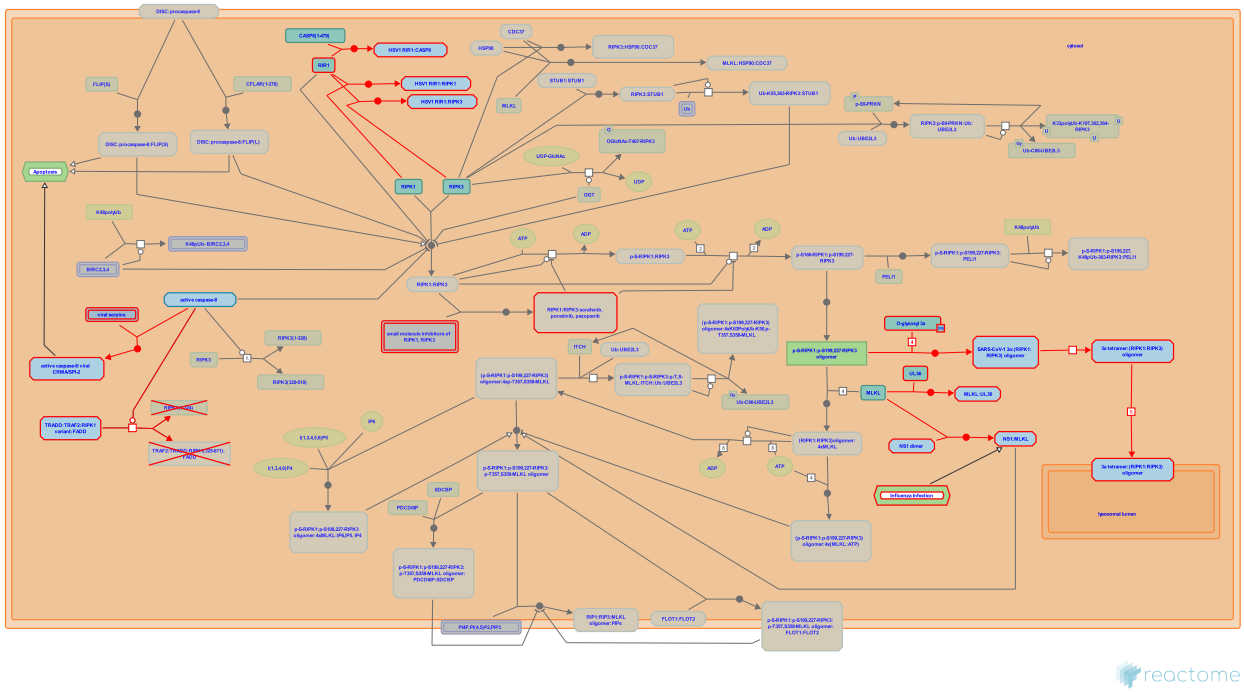
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Defective RIPK1-mediated regulated necrosis ↗

Stable identifier: R-HSA-9693928

Diseases: genetic disease



Receptor Interacting Serine/Threonine Kinase 1 (RIPK1)-mediated regulated necrosis also called necroptosis is an important type of programmed cell death in addition to apoptosis. Necroptosis eventually leads to cell lysis and release of cytoplasmic content into the extracellular region. Necroptosis must be tightly controlled. Disregulated or defective necroptotic cell death is often associated with a tissue damage resulting in an intense inflammatory response. Defects of necroptosis may contribute to various pathological processes, including autoimmune disease, neurodegeneration, multiple cancers, and kidney injury.

Literature references

Najafov, A., Shan, B., Yuan, J., Pan, H. (2018). Necroptosis in development and diseases. *Genes Dev., 32,* 327-340. ↗

Editions

2020-06-26	Reviewed	D'Eustachio, P.
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2020-08-17	Edited	Shamovsky, V.
2020-08-20	Reviewed	Lalaoui, N.

RIPK1 variant is not cleaved by CASP8 ↗

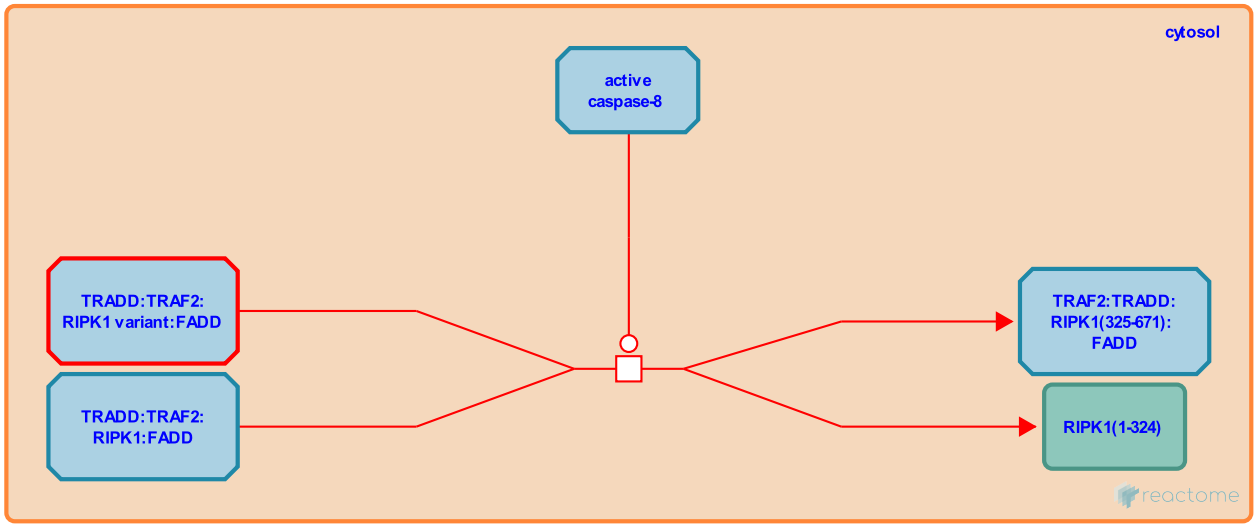
Location: Defective RIPK1-mediated regulated necrosis

Stable identifier: R-HSA-9693929

Type: transition

Compartments: cytosol

Diseases: genetic disease



Activation of receptor-interacting serine/threonine-protein kinase 1 (RIPK1) controls tumor necrosis factor receptor (TNFR)- and pattern recognition receptors-mediated apoptosis, necroptosis and inflammatory pathways. RIPK1 activity is regulated post-translationally by ubiquitylation and phosphorylation events, as well as by caspase-8 (CASP8)-mediated cleavage. CASP8 facilitates the cleavage of human and mouse RIPK1 after residues D324 and D325, respectively and prevents caspase-8-dependent apoptosis and RIPK1:RIPK3-dependent necroptosis (Lin Y et al. 1999; Hopkins-Donaldson S et al. 2000; Newton K et al. 2019; Zhang X et al. 2019; Lalaoui N et al. 2020). The dominantly inherited mutations D324N, D324H, D324V and D324Y in RIPK1 prevent CASP8 from cleaving the mutated protein, thereby promoting activation of RIPK1 and leading to an autoinflammatory response in humans (Tao P et al. 2020; Lalaoui N et al. 2020).

Literature references

Devin, A., Liu, ZG., Lin, Y., Rodriguez, Y. (1999). Cleavage of the death domain kinase RIP by caspase-8 prompts TNF-induced apoptosis. *Genes Dev., 13*, 2514-26. ↗

Editions

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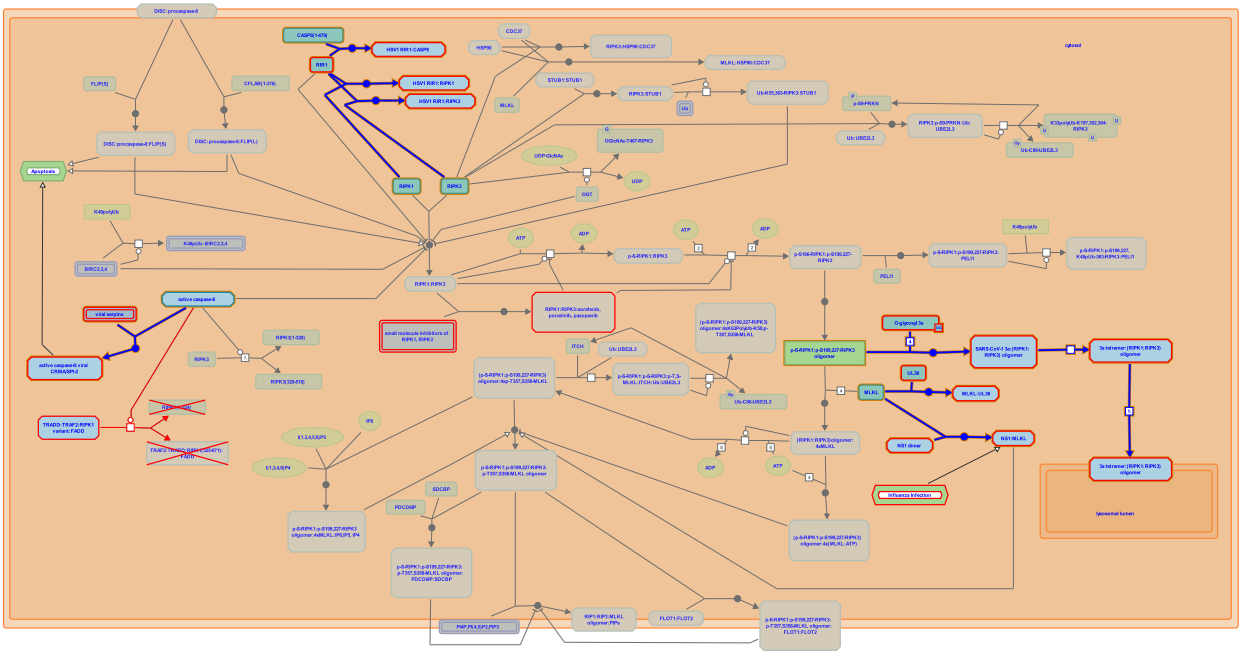
Microbial modulation of RIPK1-mediated regulated necrosis ↗

Location: Defective RIPK1-mediated regulated necrosis

Stable identifier: R-HSA-9686347

Diseases: bacterial infectious disease, viral infectious disease



Activation of receptor-interacting serine/threonine protein (RIP) kinases RIPK1 and RIPK3 coordinate an immunogenic form of programmed cell death known as regulated necrosis or necroptosis (Upton JW et al. 2017). This form of necrosis leads to anti-viral inflammation in host through cell death-associated release of damage-associated molecular patterns (DAMPs) (Nailwal H & Ka-Ming Chan F 2019; Upton JW et al. 2017). Microbial pathogens are able to modulate host regulated necrosis through different triggers and pathways. The promotion and inhibition of host cell death vary and depend on the microbe types, virulence, and phenotypes (Upton JW et al. 2010, 2012, 2017; Jaclyn S Pearson JS et al. 2017; Petrie EJ et al. 2019; Fletcher-Etherington A et al. 2020; Nailwal H & Ka-Ming Chan F 2019;).

Editions

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