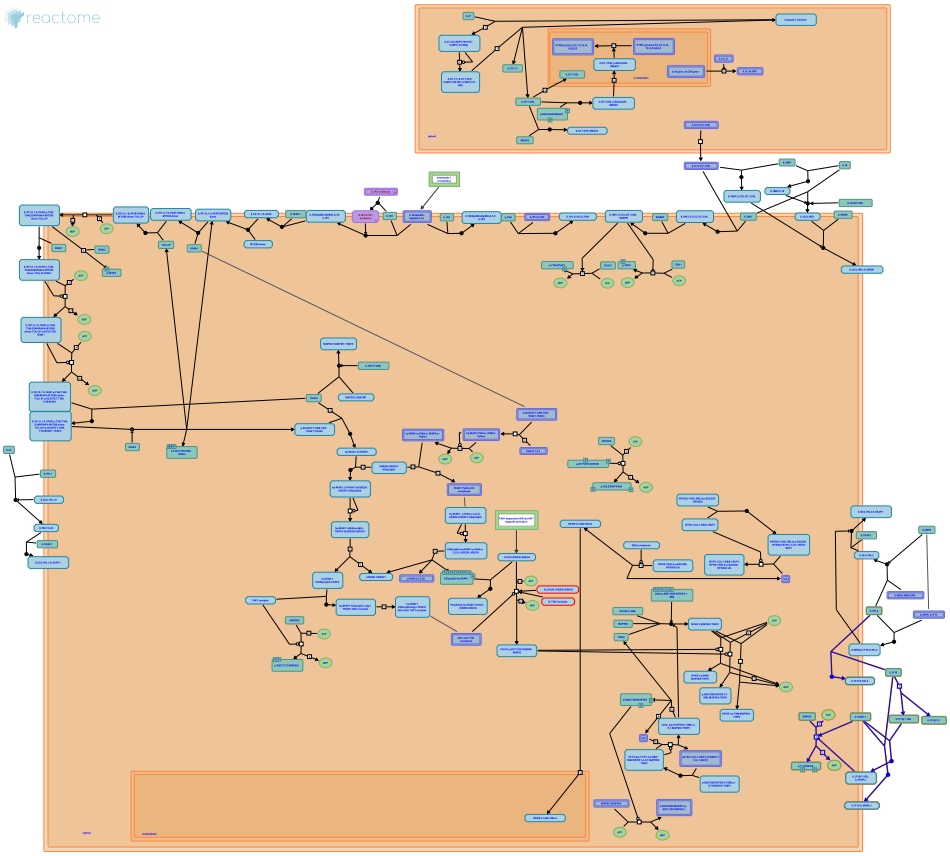
Interleukin-38 signaling



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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. ↗

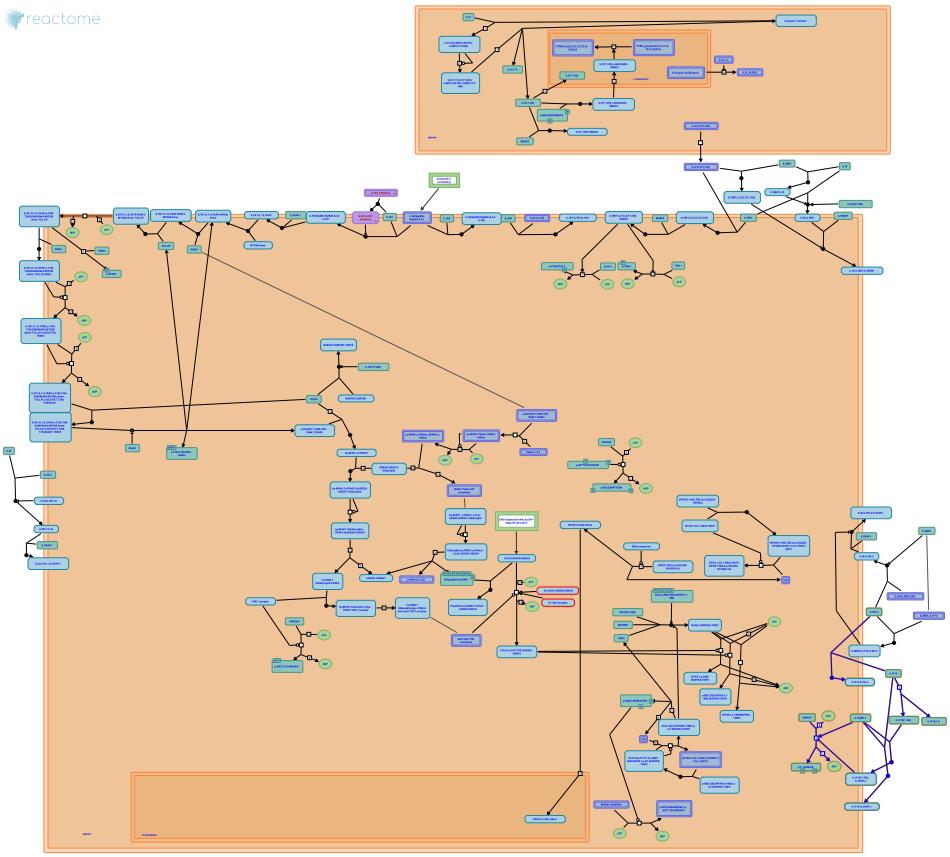
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Interleukin-38 signaling ↗

Stable identifier: R-HSA-9007892

Compartments: cytosol, extracellular region, nucleoplasm



Interleukins are immunomodulatory proteins that elicit a wide array of responses in cells and tissues. Interleukin 1 family member 10 (IL1F10, IL 38) is a member of the IL1 family (Lin et al. 2001, Bensen et al. 2001). IL1F10 is selectively produced by human apoptotic cells (Mora et al. 2016) and human epidermal keratinocytes (based on mRNA studies) (Boutet M A et al. 2016). IL1F10 can bind to interleukin 1 receptor like 2 (IL1RL2) and may result in the suppression of IL 17 and IL 22 and induction of IL 6 production (van de Veerdonk et al. 2012, Mora et al. 2016). IL1F10 is synthesized as precursors that require N terminal processing to attain full receptor agonist or antagonist function (Mora et al. 2016). Both full length (1 – 152 amino acids) and N terminal truncated (20 – 152 amino acids) IL1F10 can bind Interleukin 1 receptor accessory protein like 1 (IL1RAPL1) (Mora et al. 2016). The binding affinity of truncated IL1F10 is much higher than that of the full length. However, binding of the full length or truncated forms has distinct outcomes; the former induces IL6 and the latter suppresses IL6 via JNK and AP1 signaling (Mora et al. 2016).

Literature references

Born, TL., Garka, KE., Renshaw, BR., Smith, DE., Bertles, JS., Sims, JE. (2000). Identification and characterization of two members of a novel class of the interleukin-1 receptor (IL-1R) family. Delineation of a new class of IL-1R-related proteins based on signaling. *J. Biol. Chem., 275*, 29946-54. ↗

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Dawson, PA., Mychaleckyj, JC., Bowden, DW., Bensen, JT. (2001). Identification of a novel human cytokine gene in the interleukin gene cluster on chromosome 2q12-14. *J. Interferon Cytokine Res., 21*, 899-904. ↗

Weigert, A., Putyrski, M., Frank, AC., Wittig, I., Brüne, B., Schlemmer, A. et al. (2016). Interleukin-38 is released from apoptotic cells to limit inflammatory macrophage responses. *J Mol Cell Biol.* ↗

Editions

2017-07-28	Reviewed	Mora, J.
2017-08-08	Authored, Edited	Varusai, TM.

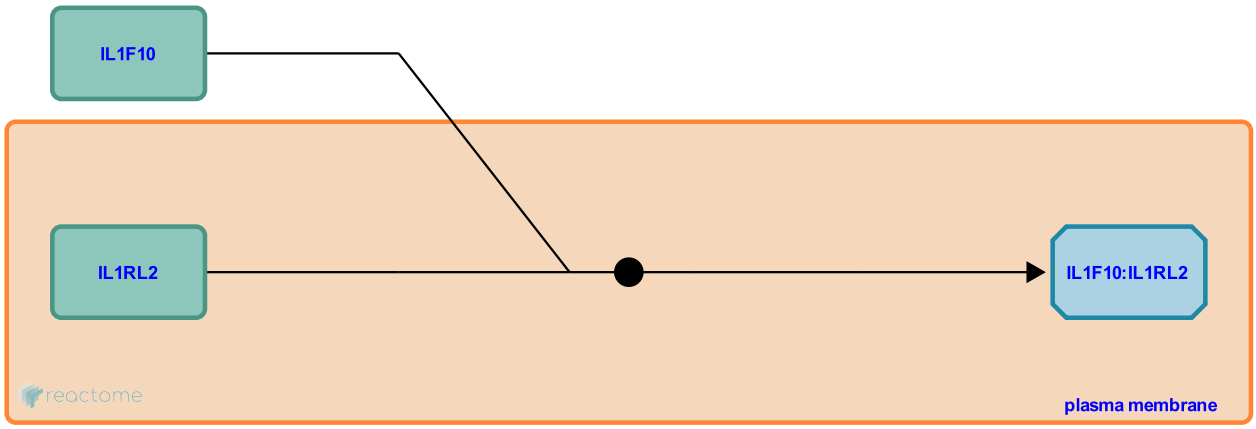
IL1F10 binds IL1RL2 ↗

Location: Interleukin-38 signaling

Stable identifier: R-HSA-9007901

Type: binding

Compartments: plasma membrane, extracellular region



Interleukins are immunomodulatory proteins that elicit a wide array of responses in cells and tissues. Interleukin 1 family member 10 (IL1F10, IL 38) is a member of the IL1 family (Lin et al. 2001, Bensen et al. 2001). IL1F10 is produced in Human apoptotic cells (Mora et al. 2016) and human epidermal keratinocytes (based on mRNA studies) (Boutet M A et al. 2016). IL1F10 can bind to interleukin 1 receptor like 2 (IL1RL2, IL 36R, IL1Rrp2, IL1R6). This binding has biological consequences similar to another IL1RL2 ligand IL 36 receptor antagonist (IL 36Ra), such as suppression of IL17 and IL22 and induction of IL6 production (van de Veerdonk et al. 2012, Mora et al. 2016). Ultimately, these events lead to suppression of cytokine production in several types of immune cells resulting in reduced inflammation.

Literature references

Dinarello, CA., Netea, MG., Azam, T., Wu, G., van de Veerdonk, FL., Hao, R. et al. (2012). IL-38 binds to the IL-36 receptor and has biological effects on immune cells similar to IL-36 receptor antagonist. *Proc. Natl. Acad. Sci. U.S.A. , 109*, 3001-5. ↗

Weigert, A., Putyrski, M., Frank, AC., Wittig, I., Brüne, B., Schlemmer, A. et al. (2016). Interleukin-38 is released from apoptotic cells to limit inflammatory macrophage responses. *J Mol Cell Biol.* ↗

Editions

2017-07-21	Authored, Edited	Varusai, TM.
2017-07-28	Reviewed	Mora, J.

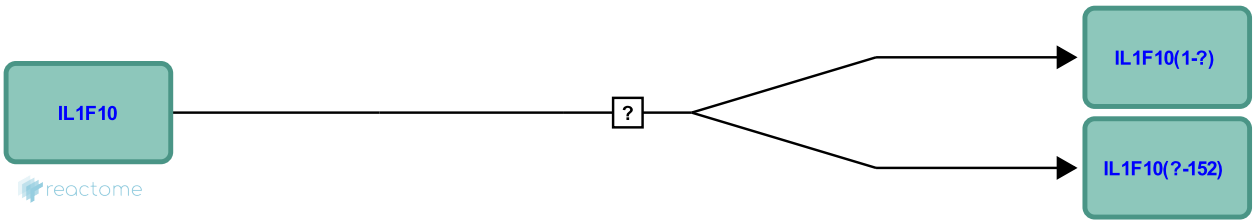
IL1F10 is cleaved ↗

Location: Interleukin-38 signaling

Stable identifier: R-HSA-9007882

Type: uncertain

Compartments: extracellular region



Interleukins are immunomodulatory proteins that elicit a wide array of responses in cells and tissues. Interleukin 1 family member 10 (IL1F10, IL 38) is a member of the IL1 family (Lin et al. 2001, Bensen et al. 2001). IL1F10 is produced in Human apoptotic cells (Mora et al. 2016) and human epidermal keratinocytes (based on mRNA studies) (Boutet M A et al. 2016). Like several other IL1 family members, IL1F10 is synthesized as precursors that require N terminal processing to attain full receptor agonist or antagonist function. The N terminal truncation of IL1F10 precursor occurs during apoptosis and the predicted cleavage site is at amino acid 19 (Mora et al. 2016). The proteases from apoptosis are believed to be the responsible for the cleavage process. This truncated form of IL1F10 may undergo additional processing before becoming an active interleukin. This event is a black box because the precise cleavage site of IL1F10 and requirement of additional processing steps are uncertain.

Followed by: IL1F10(?-152) binds IL1RAPL1

Literature references

Weigert, A., Putyrski, M., Frank, AC., Wittig, I., Brüne, B., Schlemmer, A. et al. (2016). Interleukin-38 is released from apoptotic cells to limit inflammatory macrophage responses. *J Mol Cell Biol.* ↗

Editions

2017-07-21	Authored, Edited	Varusai, TM.
2017-07-28	Reviewed	Mora, J.

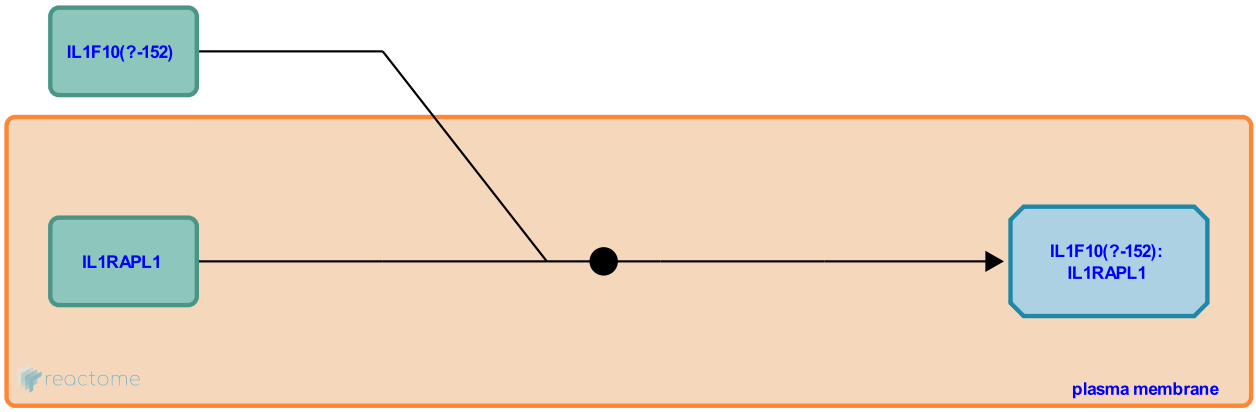
IL1F10(?-152) binds IL1RAPL1 ↗

Location: Interleukin-38 signaling

Stable identifier: R-HSA-9008052

Type: binding

Compartments: plasma membrane, extracellular region



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Preceded by: IL1F10 is cleaved

Literature references

Weigert, A., Putyrski, M., Frank, AC., Wittig, I., Brüne, B., Schlemmer, A. et al. (2016). Interleukin-38 is released from apoptotic cells to limit inflammatory macrophage responses. *J Mol Cell Biol.* ↗

Editions

2017-07-21	Authored, Edited	Varusai, TM.
2017-07-28	Reviewed	Mora, J.

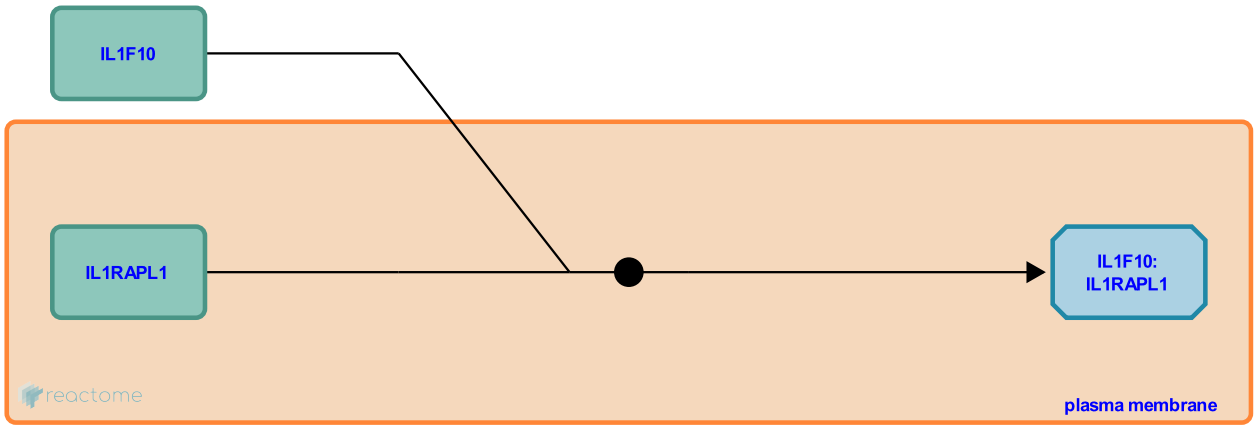
IL1F10 binds IL1RAPL1 ↗

Location: Interleukin-38 signaling

Stable identifier: R-HSA-9008054

Type: binding

Compartments: plasma membrane, extracellular region



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Followed by: MAPK8 phosphorylation

Literature references

Weigert, A., Putyrski, M., Frank, AC., Wittig, I., Brüne, B., Schlemmer, A. et al. (2016). Interleukin-38 is released from apoptotic cells to limit inflammatory macrophage responses. *J Mol Cell Biol.* ↗

Editions

2017-07-21	Authored, Edited	Varusai, TM.
2017-07-28	Reviewed	Mora, J.

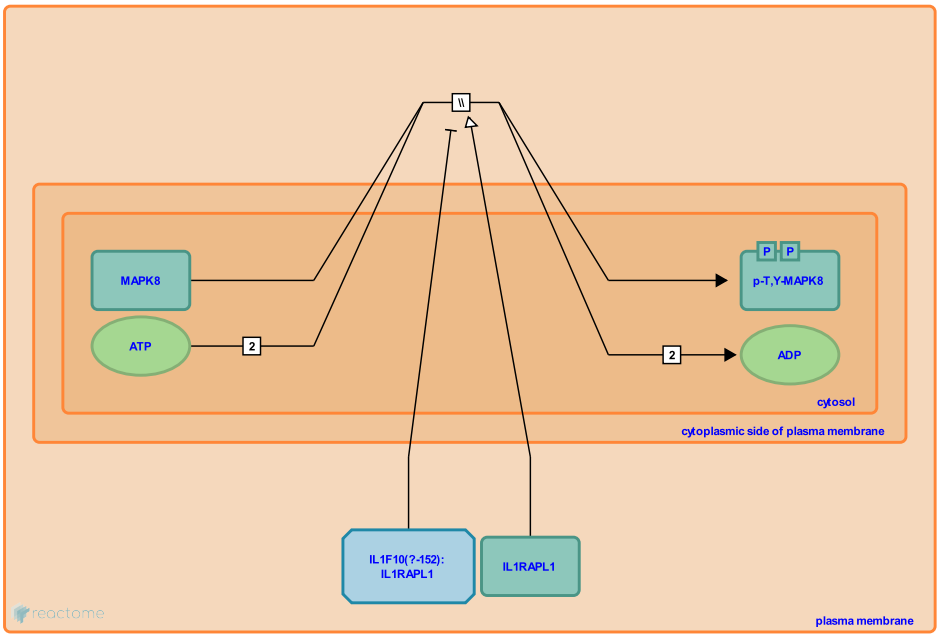
MAPK8 phosphorylation ↗

Location: Interleukin-38 signaling

Stable identifier: R-HSA-9008043

Type: omitted

Compartments: plasma membrane, extracellular region, cytosol



Interleukin 1 family member 10 (IL1F10, IL 38) is a member of the IL1 family (Lin et al. 2001, Bensen et al. 2001). IL1F10 can bind with X linked interleukin 1 receptor accessory protein like 1 (IL 1RAPL 1) (Mora et al. 2016). Stimulated IL1RAPL1 can activate Mitogen Activated Protein Kinase 8 (MAPK8, JNK1) signaling, which is required for transcription factor AP 1 activation (Born T L et al. 2000, Khan J A et al. 2004). Full length (1 – 152 amino acids) and N terminal truncated (20 – 152 amino acids) IL1F10 can bind with IL1RAPL1. The binding affinity of truncated IL1F10 is much higher than that of the full length. Binding of truncated IL1F10 to IL1RAPL1 results in inhibition of JNK signaling, which consequently leads to IL6 suppression (Mora et al. 2016). This is represented as a black box event because the mechanism of MAPK8 activation by IL1RAPL1 is uncertain.

Preceded by: IL1F10 binds IL1RAPL1

Literature references

Born, TL., Garka, KE., Renshaw, BR., Smith, DE., Bertles, JS., Sims, JE. (2000). Identification and characterization of two members of a novel class of the interleukin-1 receptor (IL-1R) family. Delineation of a new class of IL-1R-related proteins based on signaling. *J. Biol. Chem., 275*, 29946-54. ↗

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Editions

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2017-07-28	Reviewed	Mora, J.

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