Interleukin-1 family are secreted

D'Eustachio, P., Jupe, S., Kanneganti, TD., Pinteaux, E., Ray, KP., Shao, F.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

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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.

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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. ↗

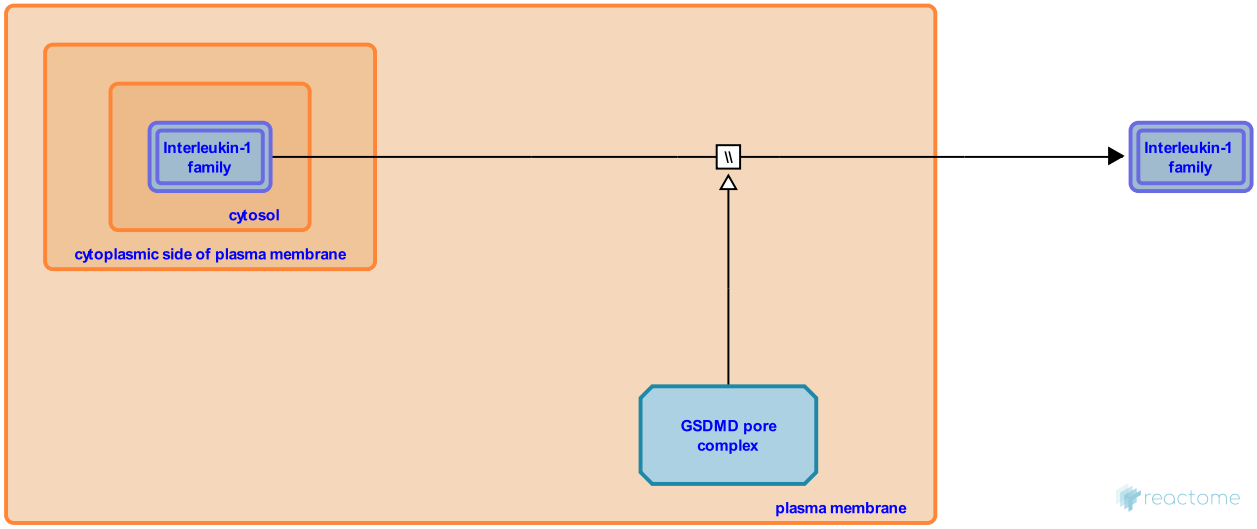
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

Interleukin-1 family are secreted ↗

Stable identifier: R-HSA-449058

Type: omitted

Compartments: plasma membrane



Interleukin-1β (IL-1β) lacks signal sequences for compartmentation within the Golgi and classical secretory vesicles, so release of the mature form to extracellular compartments requires nonclassical mechanisms of secretion which are poorly understood (Eder C 2009; Piccioli P & Rubartelli A 2013). Several secretory pathways were proposed involving secretory lysosomes, exosomes, microvesicles, and autophagic vesicles, possibly through a mechanism similar to chaperone-mediated autophagy (CMA) (Andrei C et al. 2004; Ward JR et al. 2010; MacKenzie A et al. 2001; Gudipaty L et al. 2003; Qu Y et al. 2007; Iula L et al. 2018: reviewed by Eder C 2009; Piccioli P & Rubartelli A 2013; Claude-Taupin A et al. 2018). Further, the route of IL-1β secretion was found to be dependent on the type and strength of the inflammatory stimuli (Semino C et al. 2018; Sitia R & Rubartelli A 2018). Thus, in primary human monocytes small trauma or low pathogen load (LPS) activated a pathway involving secretory lysosomes that allows slow release of IL-1β, followed by apoptotic cell death that switches off the inflammatory response (Semino C et al. 2018). Differently, a stronger stimulus (LRZ) resulted in gasdermin D (GSDMD) cleavage with generation of the N-terminal domain that assembles in N-rings with formation of pores through which IL-1β can be externalized: this pathway of secretion is followed by pyroptosis, with membrane ruptures through which DAMPs can leave cells, further amplifying the inflammatory response (Semino C et al. 2018). Caspase-8 and FADD are required for NLRP3 inflammasome activation and IL-1β release (Gurung P et al. 2014, 2016).

Literature references

Franchi, L., Nunez, G., Qu, Y., Dubyak, GR. (2007). Nonclassical IL-1 beta secretion stimulated by P2X7 receptors is dependent on inflammasome activation and correlated with exosome release in murine macrophages. *J Immunol , 179*, 1913-25. ↗

Editions

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