# Interleukin-1 family precursors are cleaved by caspase-1

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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

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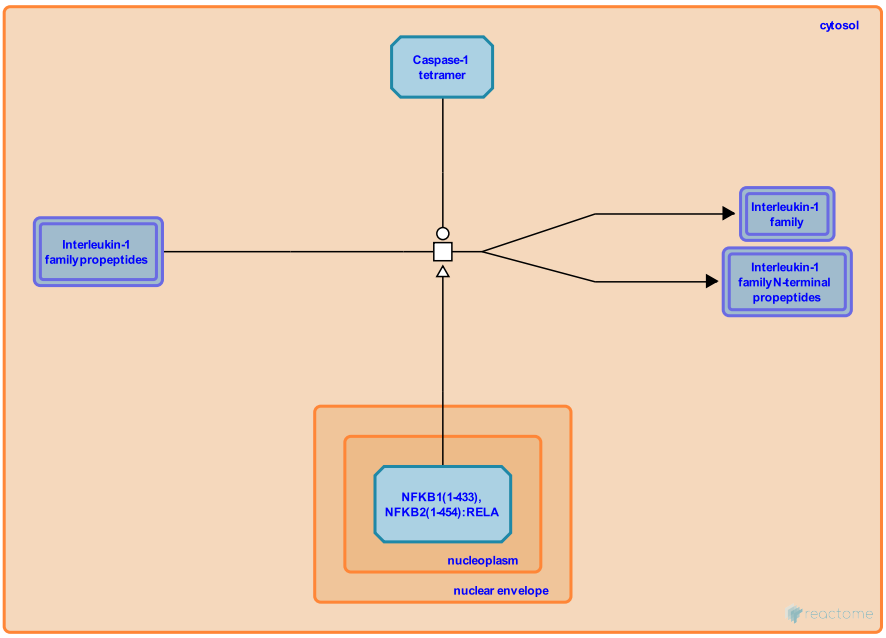
## Interleukin-1 family precursors are cleaved by caspase-1 ↗

**Stable identifier:** R-HSA-448703

**Type:** transition

**Compartments:** cytosol




In the absence of TLR agonist 'priming', inflammasome dependent caspase-1 activation is observed but IL-1 beta secretion is minimal because pro-IL1 beta is not expressed in most cells until stimulated by proinflammatory signals such as TNF or LPS that activate NFkappaB. NFkappaB induces expression of pro-IL1beta but also expression of NLRP3 which may be a limiting component of the NLRP3 inflammasome complex.
Pro-interleukin-1 beta (pro-IL1B) is the primary substrate of caspase-1. IL1B production and processing is stimulated when pathogen-associated molecular patterns (PAMPs) such as bacterial LPS are detected by cells of the innate immune system, and in response to pro-inflammatory cytokines such as TNF. Detection of PAMPs by Toll receptors leads to rapid IL1 transcription/translation and subsequent processing by caspase-1 in macrophages and monocytes. Processing is triggered by the activation of members of the NLR family and their associated inflammasome complexes. IL1B lacks a signal peptide to direct it to the Golgi for subsequent secretion, so the mode of secretion is uncertain. Once secreted, IL1B binds membrane-bound IL1 receptors, followed by recruitment of the IL1 receptor accessory protein to form a high affinity receptor complex. Ligand induced receptor activation induces the intracellular association of a number of cytosolic adapter proteins triggering intracellular signal transduction. This series of steps facilitates the induction of nuclear factor-kappa B (NFkB) and mitogen-activated protein kinase (MAPK) activity, leading to downstream transcription of additional inflammatory cytokines, including IL1B itself. A calpain-like potease has been reported to be important for the processing of pro- IL1A, but much less is known about how IL1A is released from cells and what specific roles it plays in biology.

## Literature references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## Editions

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