SPPL2a/b cleaves TNF(1-76)

Fluhrer, R., Jupe, S.
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


Reactome database release: 78

This document contains 1 reaction (see Table of Contents)
**SPPL2a/b cleaves TNF(1-76)**

**Stable identifier:** R-HSA-8863101

**Type:** uncertain

**Compartments:** cytosol, extracellular region, plasma membrane

The peptide fragment that remains after soluble TNFalpha is released by sheddases like ADAM17 is further processed by intramembrane proteolysis, releasing an intracellular domain (ICD) into the cytoplasm and C-terminal fragments into the extracellular region (Fluhrer et al. 2006). SPP/SPPL proteins are intramembrane-cleaving aspartyl proteases. SPPL2a has been located in lysosomes/late endosomes of murine embryonic fibroblasts (Behnke et al. 2011) but when overexpressed in HeLa cells is found in significant amounts at the cell surface (Behnke et al. 2011). Overexpressed SPPL2b was detected primarily at the cell surface (Friedmann et al. 2006, Behnke et al. 2011). Overexpression or RNAi-mediated knockdown of either SPPL2a or SPPL2b in cell culture models demonstrates that both proteases are able to cleave TNFalpha (Fluhrer et al. 2006, Friedmann et al. 2006). SPPL2a/b-mediated intramembrane proteolysis of TNFalpha in bone marrow-derived dendritic cells was seen to up-regulate transcription and secretion of IL-12 (Friedmann et al. 2006). Whether TNFalpha ICD fragments can translocate to the nucleus and directly activate transcription of IL-12 gene is unknown. SPLL2a and b have a number of other substrates that suggest physiological roles within the hematopoietic system and for the regulation of inflammatory responses (Voss et al. 2013).

**Literature references**


**Editions**

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