TNF-α is cleaved by ADAM17 (TACE)

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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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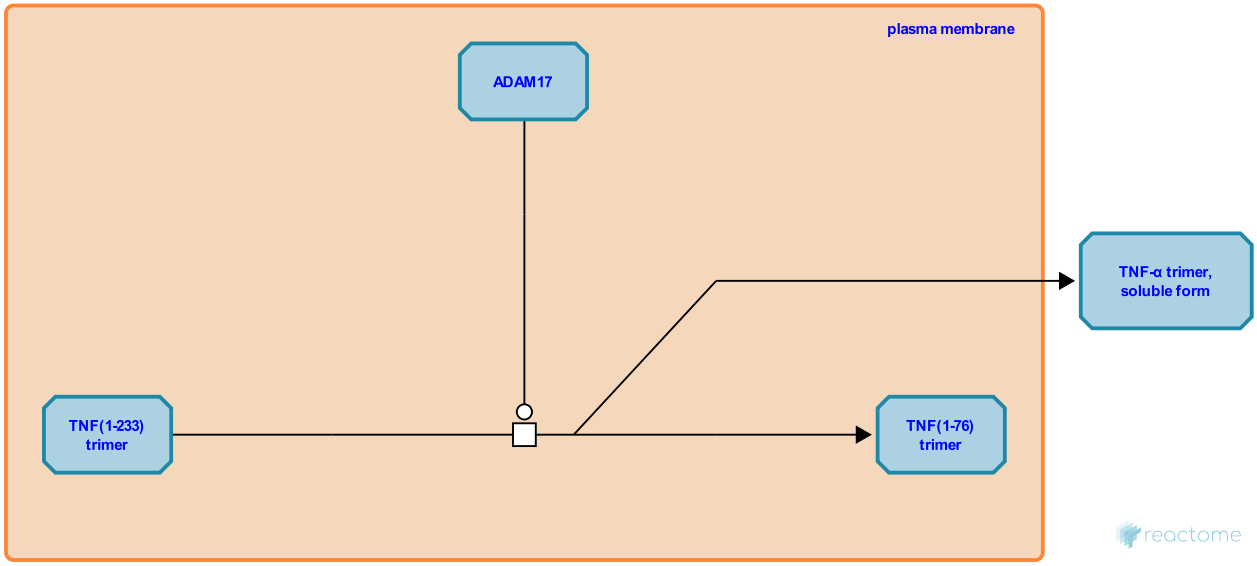
Stable identifier: R-HSA-3371385

Type: transition

Compartments: extracellular region, plasma membrane



TNF-α is initially synthesized as a 26kDa transmembrane protein (membrane TNF-α), which is processed by proteolytic cleavage known as ectodomain shedding (Tang P et al. 1996). TNF-α-converting enzyme (TACE or ADAM17) mediates the cleavage of TNF-α generating the soluble 17kDa form (Robertshaw HJ & Brennan FM 2005). Inhibition of TACE activity resulted in an accumulation of unprocessed TNF-α on the cell surface of human monocytic cells (THP1) (Tabaka HN et al. 2012). Both membrane-bound and secreted forms of TNF-α are biologically active and may trigger different activities due to their differential capacities to stimulate TNFR1 and TNFR2. TNFR1 is efficiently activated by soluble and membrane TNF-α, TNFR2 signaling, however, is preferentially stimulated by membrane TNF-α while the soluble form has limited activity on this receptor despite efficient binding (Grell M et al. 1995; Grell M et al. 1998).

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Editions

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