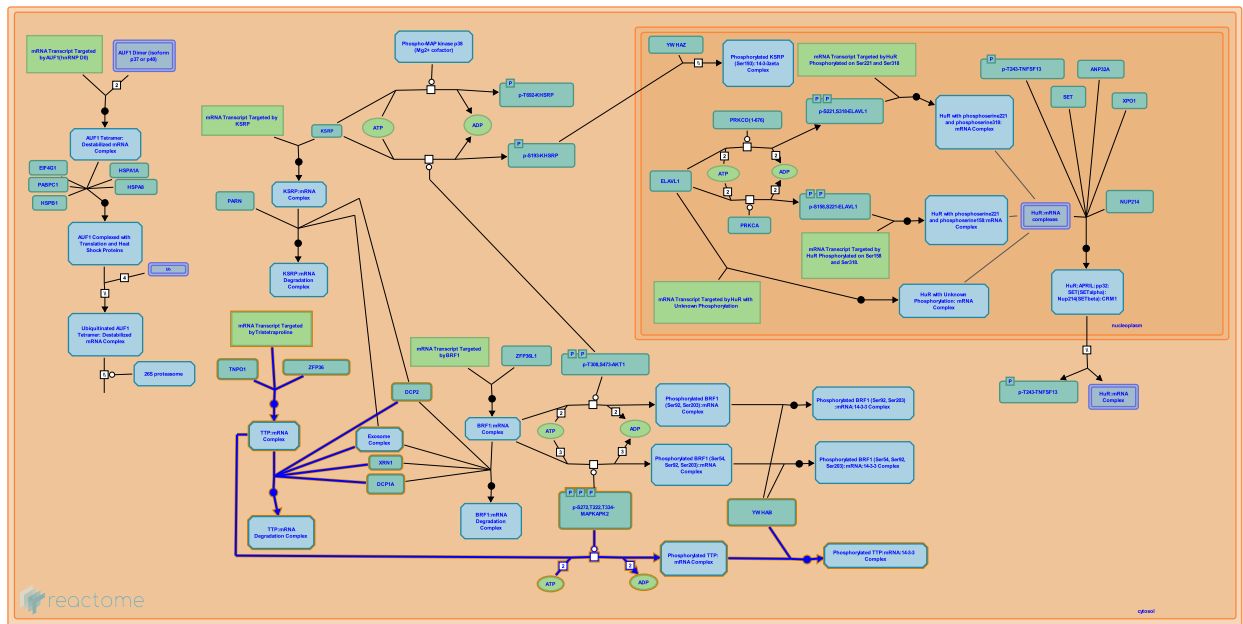


# Tristetraprolin (TTP, ZFP36) binds and destabilizes mRNA



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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the [Reactome Textbook](https://reactome.org).

02/05/2024

## 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).

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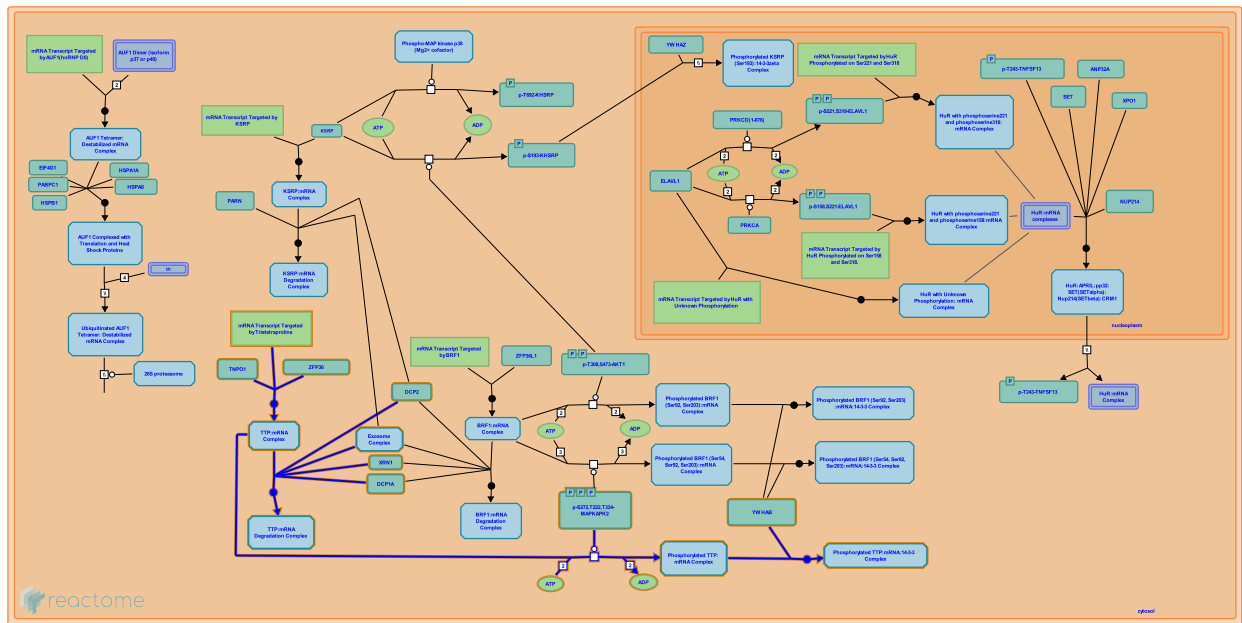
Reactome database release: 88

This document contains 1 pathway and 4 reactions ([see Table of Contents](#))

# Tristetraprolin (TTP, ZFP36) binds and destabilizes mRNA ↗

Stable identifier: R-HSA-450513

Compartments: cytosol



Tristetraproline (TTP) binds RNAs that contain AU-rich elements and recruits enzymes that degrade RNA. TTP interacts with the exosome (3' to 5' exonuclease), XRN1 (5' to 3' exonuclease), and the decapping enzymes DCP1 and DCP2a.

The activity of TTP is regulated by phosphorylation. MK2 phosphorylates TTP, which then binds 14-3-3. The interaction with 14-3-3 prevents phosphorylated TTP from entering stress granules and stabilizes mRNA bound by phosphorylated TTP. Tristetraproline is known to bind AU-rich elements in the following mRNAs: Tumor necrosis factor alpha (TNFA), Granulocyte-macrophage colony stimulating factor (CSF2, GM-CSF), Interleukin-2 (IL-2), and Proto-oncogene C-FOS (FOS, c-fos). Mice deficient in TTP exhibit arthritis, weight loss, skin lesions, autoimmunity, and myeloid hyperplasia.

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## Editions

2009-12-29	Authored, Edited	May, B.
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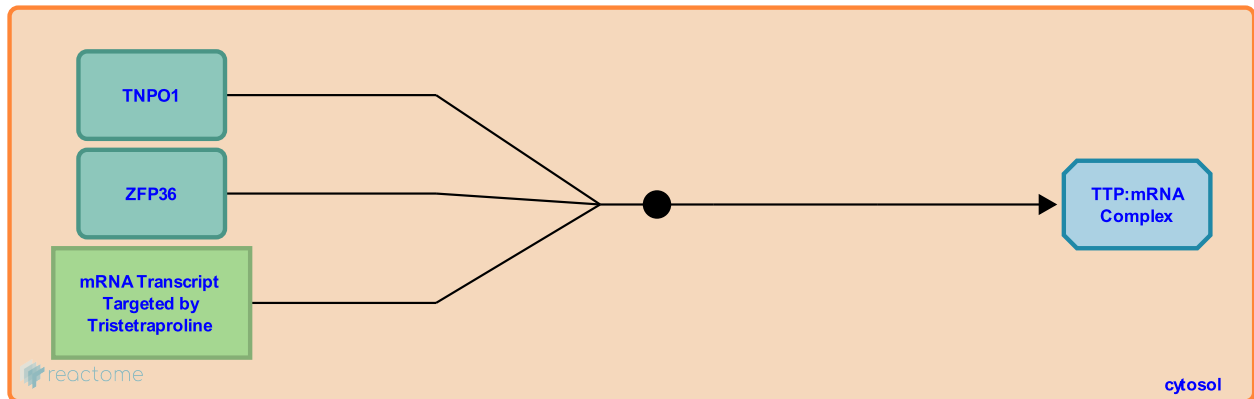
## ZFP36 (Tristetraprolin, TTP) binds AU-rich elements in 3' UTR of target mRNAs ↗

**Location:** [Tristetraprolin \(TTP, ZFP36\) binds and destabilizes mRNA](#)

**Stable identifier:** R-HSA-450400

**Type:** binding

**Compartments:** cytosol



Tristetraprolin (TTP) binds UUAUUUAUU motifs in the AU-rich elements of mRNAs. TTP binds Transportin-1 (Importin beta-2) which plays a role in shuttling TTP between P-bodies and stress granules.

**Followed by:** [MK2 phosphorylates ZFP36 \(Tristetraprolin, TTP\), ZFP36 \(TTP\) recruits RNA degradation activities](#)

### Literature references

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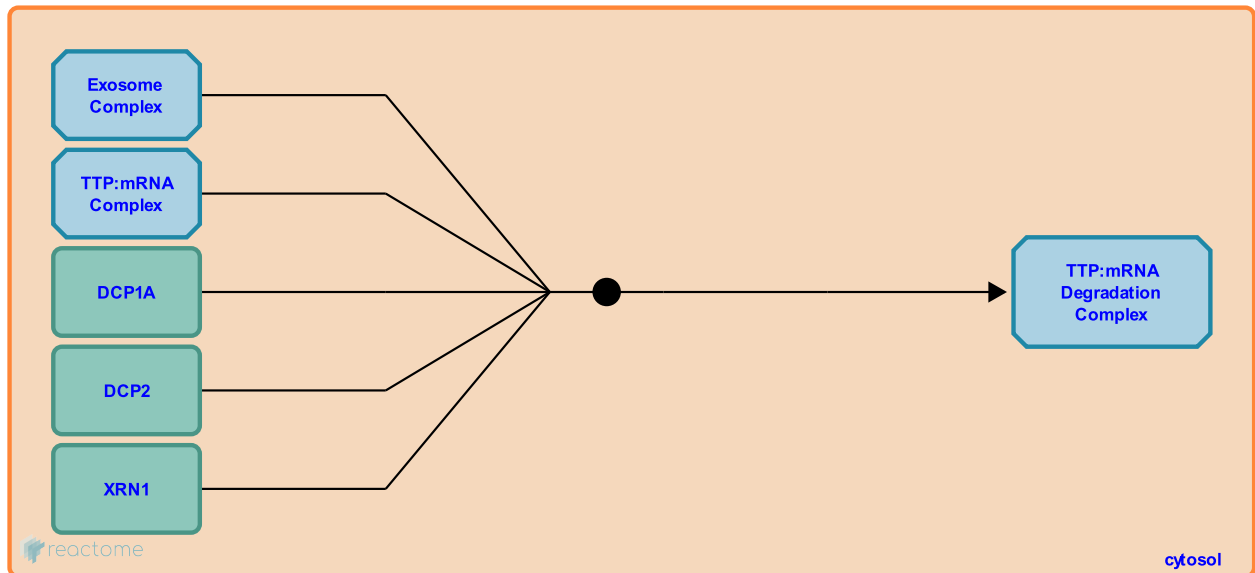
## ZFP36 (TTP) recruits RNA degradation activities ↗

**Location:** [Tristetraprolin \(TTP, ZFP36\) binds and destabilizes mRNA](#)

**Stable identifier:** R-HSA-450431

**Type:** binding

**Compartments:** cytosol



TTP interacts directly with exonucleases (XRN1 and the exosome) and decapping enzymes (DCP1a and DCP2) which hydrolyze the mRNA bound by TTP. TTP also recruits PARN deadenylase, however a direct interaction between TTP and PARN has not been demonstrated.

**Preceded by:** [ZFP36 \(Tristetraproline, TTP\) binds AU-rich elements in 3' UTR of target mRNAs](#)

### Literature references

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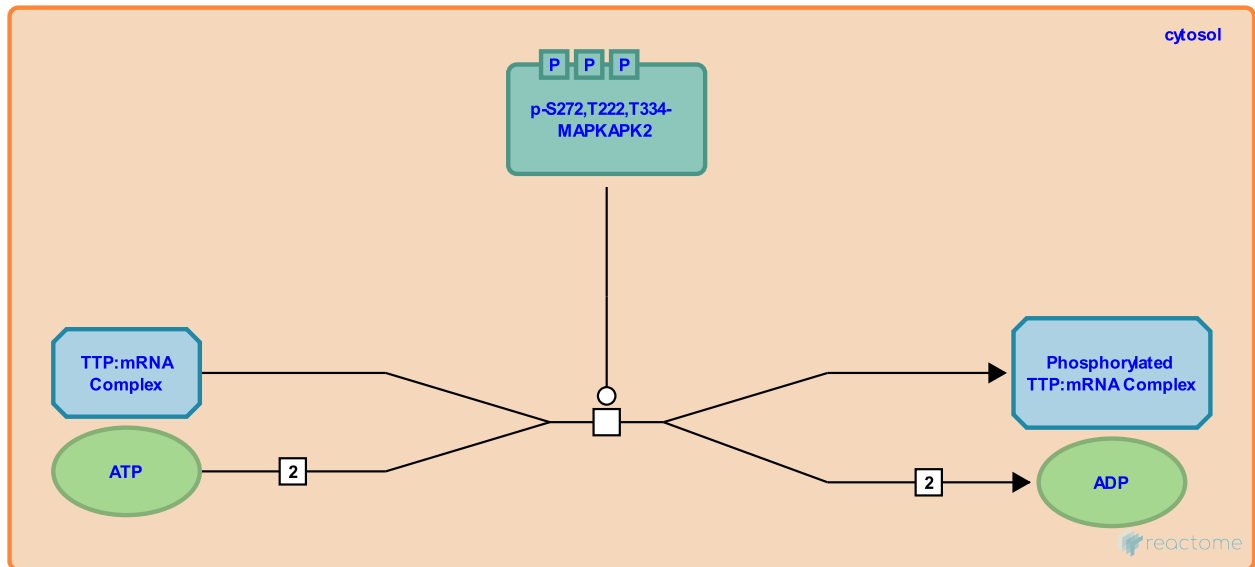
## MK2 phosphorylates ZFP36 (Tristetraproline, TTP) ↗

**Location:** Tristetraproline (TTP, ZFP36) binds and destabilizes mRNA

**Stable identifier:** R-HSA-450463

**Type:** transition

**Compartments:** cytosol



TTP is phosphorylated by MK2 at serines 60 and 186.

**Preceded by:** ZFP36 (Tristetraproline, TTP) binds AU-rich elements in 3' UTR of target mRNAs

**Followed by:** p-S60,S186-ZFP36 (Tristetraproline, TTP) binds 14-3-3beta

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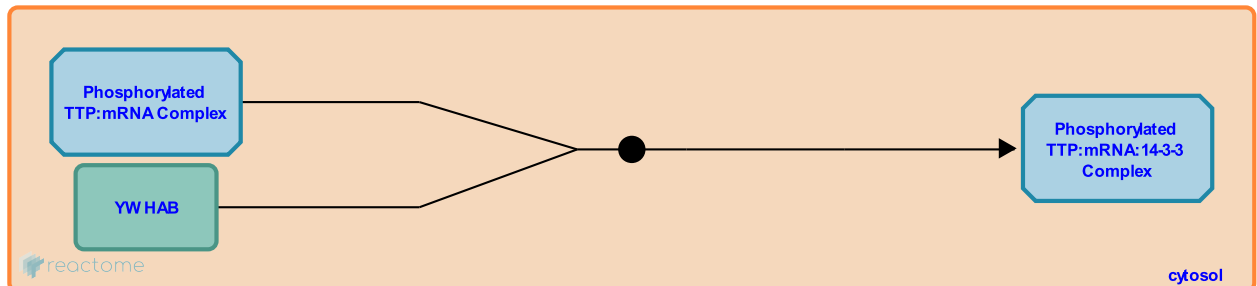
## p-S60,S186-ZFP36 (Tristetraproline, TTP) binds 14-3-3beta ↗

**Location:** [Tristetraproline \(TTP, ZFP36\) binds and destabilizes mRNA](#)

**Stable identifier:** R-HSA-450394

**Type:** binding

**Compartments:** cytosol



Phosphorylated tristetraproline (TTP) binds 14-3-3, which inhibits the ability of TTP to destabilize RNA. Thus RNAs bound by TTP become stabilized. The binding of 14-3-3 causes TTP to be excluded from stress granules.

**Preceded by:** [MK2 phosphorylates ZFP36 \(Tristetraproline, TTP\)](#)

### Literature references

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