# NFKB p105, TPL2 (COT) and ABIN2 form a stable complex

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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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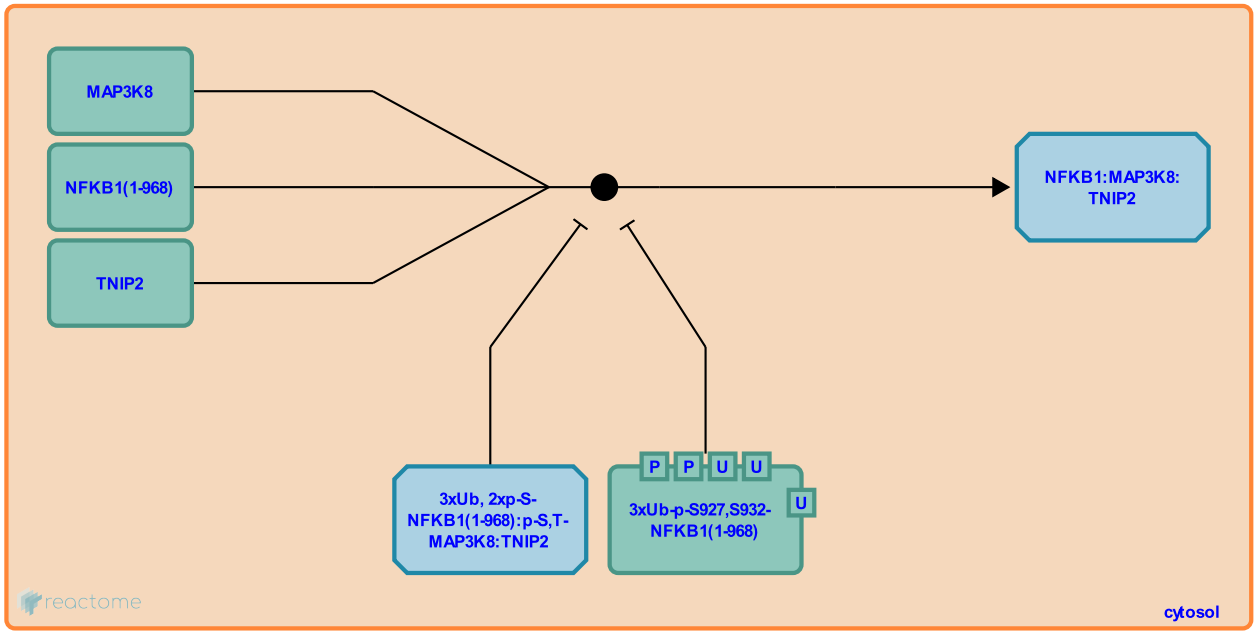
## NFKB p105, TPL2 (COT) and ABIN2 form a stable complex ↗

**Stable identifier:** R-HSA-451634

**Type:** binding

**Compartments:** cytosol




Degradation of NFKB p105 frees Tpl2 from p105 allowing it to activate MEK1.
The C-terminal half of NFKB1 p105 forms a high-affinity stoichiometric association with MAP3K8 (TPL2) via two distinct interactions (Belich et al. 1999; Beinke et al. 2003). The Tpl2 C-terminus (residues 398-467) binds to a region N-terminal to the p105 ankyrin repeat region (human p105 residues 497-534), whereas the Tpl2 kinase domain interacts with the p105 death domain (Beinke et al. 2003). In unstimulated macrophages, all detectable Tpl2 is associated with p105 (Belich et al. 1999; Lang et al. 2004). Binding to p105 maintains the stability of Tpl2 but inhibits Tpl2 MEK kinase activity by preventing access to MEK (Beinke et al. 2003; Waterfield et al. 2003). Tpl2 phosphorylation at Thr-290 may also play a role in the activation of Tpl2 (Cho & Tsichlis 2005).

A20-binding inhibitor of NFkappaB2 (ABIN-2 ot TNIP2) interacts with Tpl2 and p105 but preferentially forms a ternary complex with both proteins. As ABIN2 is a polyubiquitin binding protein, it has been suggested that it may facilitate recruitment of the p105/Tpl2 complex to the activated IKK complex, allowing IKK2 induced p105 phosphorylation and consequent Tpl2 activation.

## Literature references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## Editions

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