TAK1 is activated

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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

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18*, 142. ↗

Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

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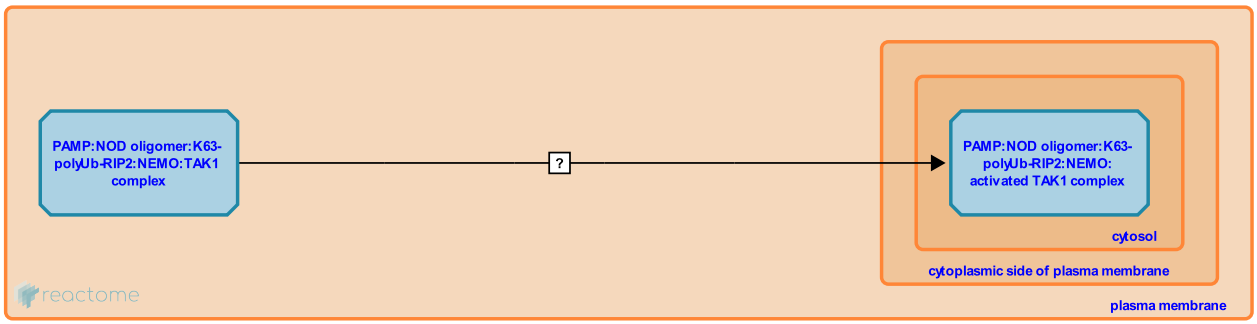
Stable identifier: R-HSA-706479

Type: uncertain

Compartments: plasma membrane, cytosol



The TAK1 complex consists of Transforming growth factor-beta (TGFB)-activated kinase (TAK1) and TAK1-binding protein 1 (TAB1), TAB2 and TAB3. TAK1 requires TAB1 for its kinase activity (Shibuya et al. 1996, Sakurai et al. 2000). TAB1 promotes TAK1 autophosphorylation at the kinase activation lobe, probably through an allosteric mechanism (Brown et al. 2005, Ono et al. 2001). The TAK1 complex is regulated by polyubiquitination. Binding of TAB2 and TAB3 to Lys63-linked polyubiquitin chains leads to the activation of TAK1 by an uncertain mechanism. Binding of multiple TAK1 complexes to the same polyubiquitin chain may promote oligomerization of TAK1, facilitating TAK1 autophosphorylation and subsequent activation of its kinase activity (Kishimoto et al. 2000). The binding of TAB2/3 to polyubiquitinated TRAF6 may facilitate polyubiquitination of TAB2/3 by TRAF6 (Ishitani et al. 2003), which might result in conformational changes within the TAK1 complex that lead to TAK1 activation. Another possibility is that TAB2/3 may recruit the IKK complex by binding to ubiquitinated NEMO; polyubiquitin chains may function as a scaffold for higher order signaling complexes that allow interaction between TAK1 and IKK (Kanayama et al. 2004).

Literature references

Shibuya, H., Gaynor, RB., Ninomiya-Tsuji, J., Takaesu, G., Ishitani, T., Matsumoto, K. (2003). Role of the TAB2-related protein TAB3 in IL-1 and TNF signaling. *EMBO J, 22*, 6277-88. ↗

Deng, L., Seth, RB., Kanayama, A., Shaito, A., Hong, M., Chiu, YH. et al. (2004). TAB2 and TAB3 activate the NF-kappaB pathway through binding to polyubiquitin chains. *Mol Cell, 15*, 535-48. ↗

Kishimoto, K., Ninomiya-Tsuji, J., Matsumoto, K. (2000). TAK1 mitogen-activated protein kinase kinase kinase is activated by autophosphorylation within its activation loop. *J Biol Chem, 275*, 7359-64. ↗

Editions

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