TLR folding by chaperones GP96 and CN-PY3

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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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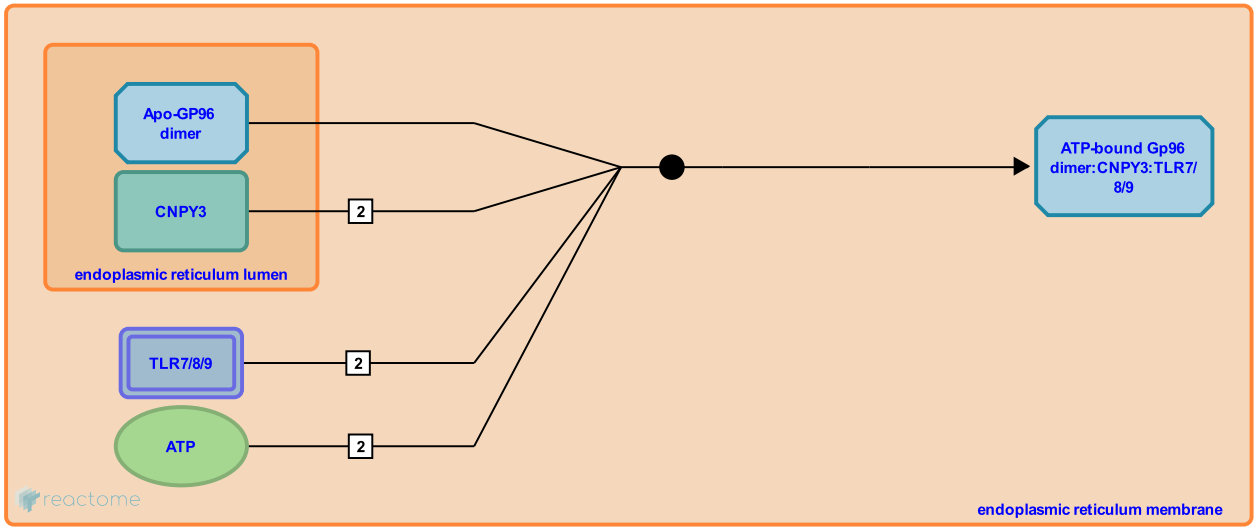
Stable identifier: R-HSA-1678923

Type: binding

Compartments: endoplasmic reticulum lumen, endoplasmic reticulum membrane



GP96 (also known as GRP94, HSP90b1), a paralogue of HSP90 in the endoplasmic reticulum, acts as a chaperone for some integrines and Toll-like receptors. Macrophages or B-cells from gp96 knockout mice have abrogated function of TLR2, 4, 5, 7 and 9, but not TLR3 (Yang Y et al 2007, Liu B and Li Z 2008, Staron M et al 2010). GP96 interacts with TLRs and integrines via its C-terminal hydrophobic domain, formed by residues 652-678 (Wu S et al 2012). GP96 functions as a V-shaped dimer in ATP-dependent manner, however it remains unclear how ATP hydrolysis-dependent conformational changes of GP96 are regulated (Li Z and Srivastava PK 1993).

GP96 forms a complex with co-chaperone CNPY3, also known as PRAT4A. GP96-CNPY3 promotes the proper post-translational ectodomain folding of TLRs, but not TLR3 (Liu B et al 2010).

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