

Dephosphorylation of CD3-zeta by PD-1 bound phosphatases

Bluestone, JA., Esensten, J., Garapati, P V.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of [Creative Commons Attribution 4.0 International \(CC BY 4.0\) License](#). For more information see our [license](#).

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).

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. [↗](#)

Reactome database release: 73

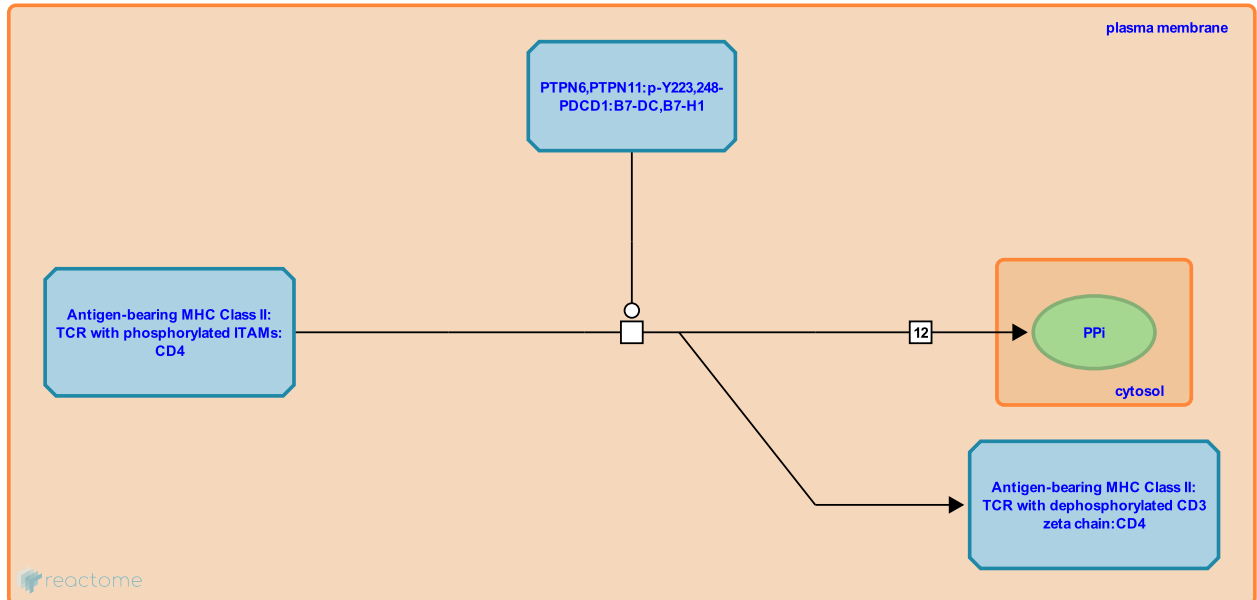
This document contains 1 reaction ([see Table of Contents](#))

Dephosphorylation of CD3-zeta by PD-1 bound phosphatases ↗

Stable identifier: R-HSA-389758

Type: transition

Compartments: plasma membrane, cytosol



PD-1 delivers inhibitory signals and downregulates antigen receptor signaling through direct dephosphorylation of signaling intermediates. The phosphatases SHP-1 and SHP-2 dephosphorylate CD3 zeta and inhibit the phosphorylation of ZAP-70 and PKC theta.

Literature references

- Keir, ME., Butte, MJ., Freeman, GJ., Sharpe, AH. (2008). PD-1 and its ligands in tolerance and immunity. *Annu Rev Immunol*, 26, 677-704. ↗
- Carter, LL., Carreno, BM. (2003). Cytotoxic T-lymphocyte antigen-4 and programmed death-1 function as negative regulators of lymphocyte activation. *Immunol Res*, 28, 49-59. ↗
- Sheppard, KA., Fitz, LJ., Lee, JM., Benander, C., George, JA., Wooters, J. et al. (2004). PD-1 inhibits T-cell receptor induced phosphorylation of the ZAP70/CD3zeta signalosome and downstream signaling to PKCtheta. *FEBS Lett*, 574, 37-41. ↗
- Fife, BT., Bluestone, JA. (2008). Control of peripheral T-cell tolerance and autoimmunity via the CTLA-4 and PD-1 pathways. *Immunol Rev*, 224, 166-82. ↗

Editions

2008-12-16	Authored, Edited	Garapati, P V.
2009-06-01	Reviewed	Bluestone, JA., Esensten, J.