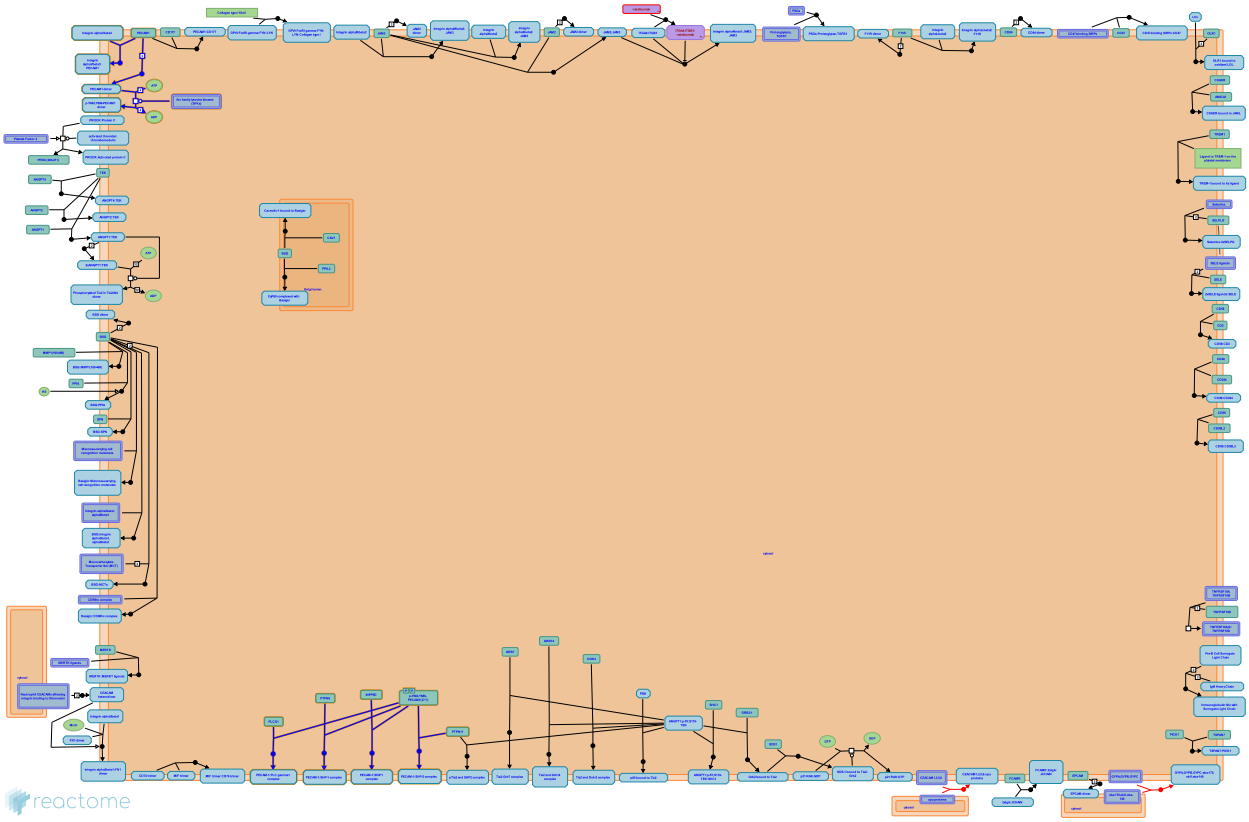
PECAM1 interactions



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

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.

29/04/2024

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).

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. ↗

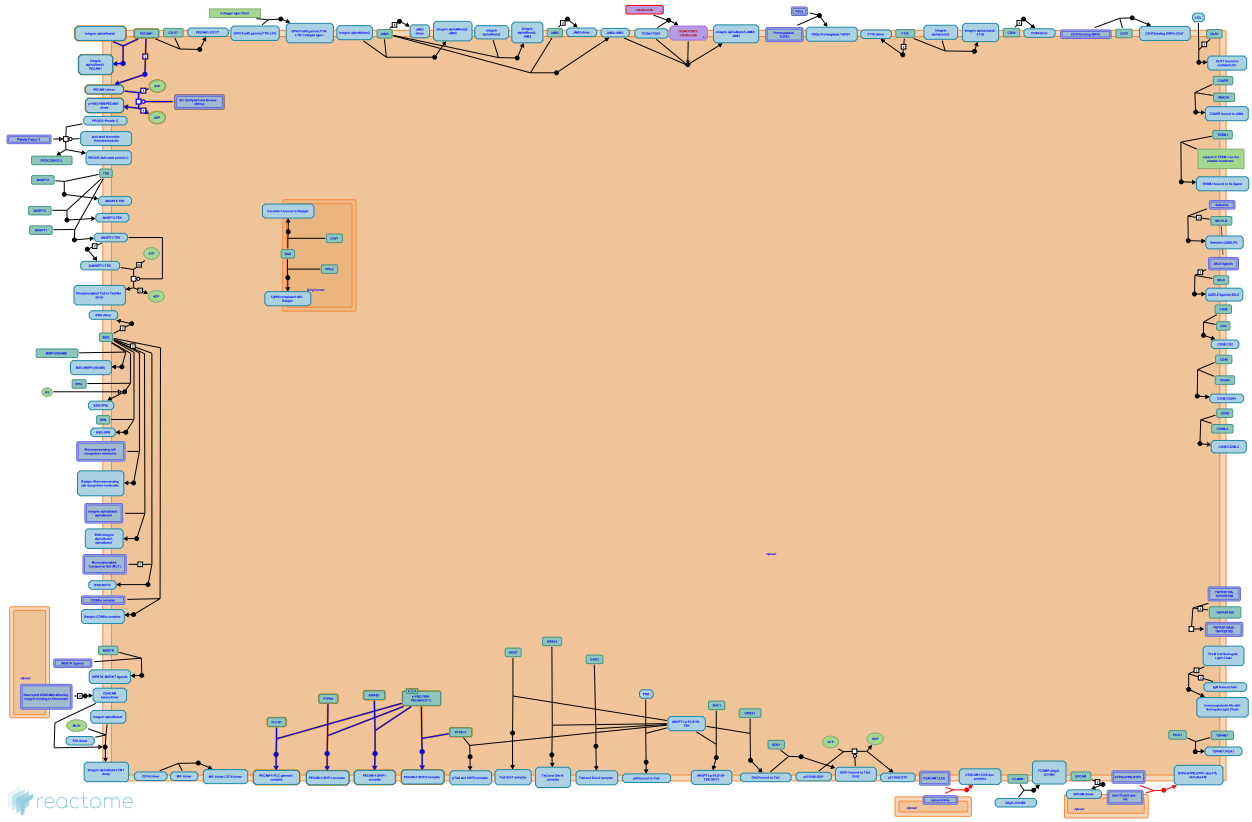
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

PECAM1 interactions ↗

Stable identifier: R-HSA-210990



PECAM-1/CD31 is a member of the immunoglobulin superfamily (IgSF) and has been implicated to mediate the adhesion and trans-endothelial migration of T-lymphocytes into the vascular wall, T cell activation and angiogenesis. It has six Ig homology domains within its extracellularly and an ITIM motif within its cytoplasmic region. PECAM-1 mediates cellular interactions by both homophilic and heterophilic interactions. The cytoplasmic domain of PECAM-1 contains tyrosine residues which serves as docking sites for recruitment of cytosolic signaling molecules. Under conditions of platelet activation, PECAM-1 is phosphorylated by Src kinase members. The tyrosine residues 663 and 686 are required for recruitment of the SH2 domain containing PTPs.

Literature references

Jackson, DE. (2003). The unfolding tale of PECAM-1. *FEBS Lett, 540*, 7-14. ↗

Gong, N., Chatterjee, S. (2003). Platelet endothelial cell adhesion molecule in cell signaling and thrombosis. *Mol Cell Biochem, 253*, 151-8. ↗

Editions

2008-02-26	Authored	de Bono, B., Garapati, P V.
2008-02-26	Reviewed	Trowsdale, J.

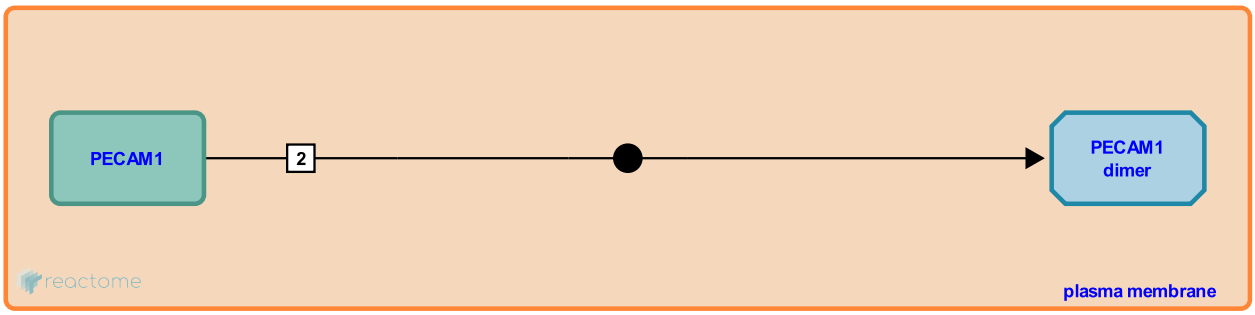
Trans-homophilic interaction of PECAM-1 ↗

Location: PECAM1 interactions

Stable identifier: R-HSA-210285

Type: binding

Compartments: plasma membrane



PECAM-mediated adhesion is complex, because it is capable of binding both to itself (homophilic adhesion) and to non-PECAM ligands (heterophilic adhesion). The trans-homophilic interaction between the two PECAM-1 molecules is mediated by their NH2-terminal membrane distal Ig homology domains 1 and 2 plus the proper spacing formed by the six Ig-homology domains.

Literature references

Buckley, CD., Simmons, DL., Harvey, DJ., Newton, JP., Hunter, AP. (1999). CD31 (PECAM-1) exists as a dimer and is heavily N-glycosylated. *Biochem Biophys Res Commun, 261*, 283-91. ↗

Buckley, CD., Jones, EY., Simmons, DL., Newton, JP. (1997). Residues on both faces of the first immunoglobulin fold contribute to homophilic binding sites of PECAM-1/CD31. *J Biol Chem, 272*, 20555-63. ↗

Editions

2008-02-26	Authored	de Bono, B., Garapati, P V.
2008-02-26	Reviewed	Trowsdale, J.

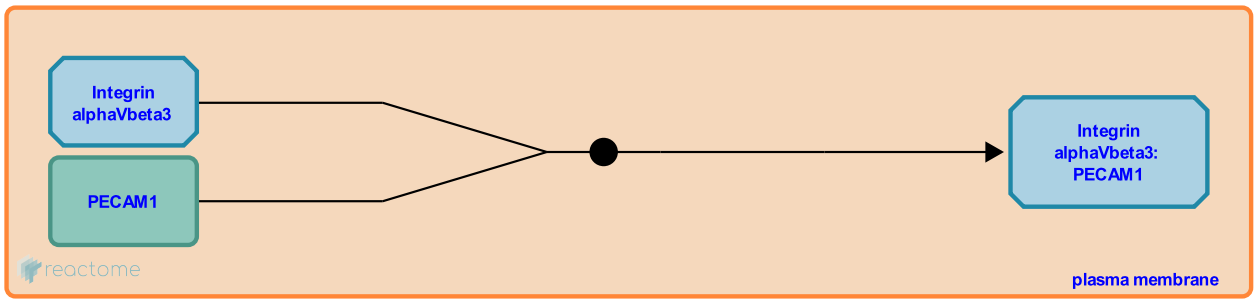
Interaction of integrin alphaVbeta3 with PECAM1 ↗

Location: PECAM1 interactions

Stable identifier: R-HSA-210304

Type: binding

Compartments: plasma membrane



Alpha v beta 3 integrin is one of the potential heterophilic ligands of PECAM-1 that is involved in down-regulation of T-cell responses. The heterophilic interaction of alpha v beta 3 integrin on endothelial cells with PEACAM-1 on leukocytes increases the adhesive function of beta integrins on T cells, monocytes, neutrophils and NK cells suggesting that leukocyte PEACAM-1 act as a signaling molecule.

Literature references

Imhof, BA., Bachmann, F., Piali, L., Uherek, C., Dunon, D., Gisler, RH. et al. (1995). CD31/PECAM-1 is a ligand for alpha v beta 3 integrin involved in adhesion of leukocytes to endothelium. *J Cell Biol, 130,* 451-60. ↗

Buckley, CD., Brown, EJ., Simmons, DL., Blystone, SD., Newton, JP., Doyonnas, R. et al. (1996). Identification of alpha v beta 3 as a heterotypic ligand for CD31/PECAM-1. *J Cell Sci, 109,* 437-45. ↗

Editions

2008-02-26	Authored	de Bono, B., Garapati, P V.
2008-02-26	Reviewed	Trowsdale, J.

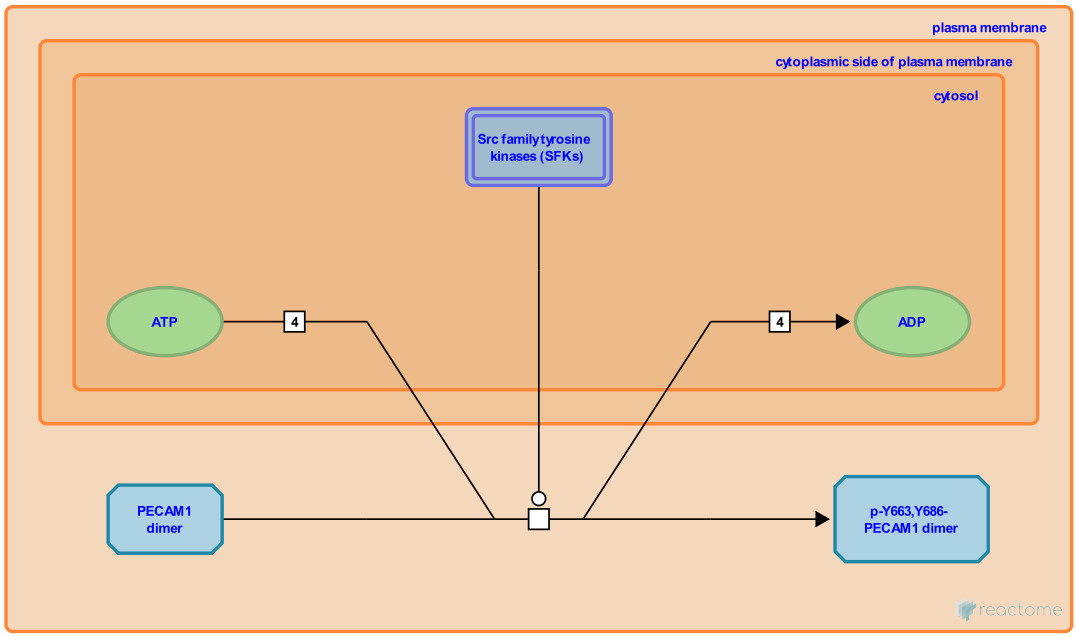
Phosphorylation of PECAM-1 by Fyn or Lyn or c-Src ↗

Location: PECAM1 interactions

Stable identifier: R-HSA-210291

Type: transition

Compartments: plasma membrane, cytosol



PECAM-1 is capable of transmitting information into the cell following its engagement and becomes tyrosine-phosphorylated during the platelet aggregation process. The Src family of tyrosine kinases (more specifically, Src, Lyn, and c-src) has been widely implicated in the phosphorylation of PECAM-1. Conserved tyrosine residues (Tyr663 and Tyr686) within the PECAM-1 cytoplasmic ITIM motif have been shown to become phosphorylated. Tyrosine phosphorylation of PECAM-1 prompts its association with intracellular signal transduction molecules.

Followed by: Interaction of PECAM-1 and SHP-1, Interaction of PECAM-1 and SHIP, Interaction of PECAM-1 and SHP-2, Interaction of PECAM-1 and PLC gamma1

Literature references

Barry, FA., Gibbins, JM., Thomas, JM., Sage, T., Cicmil, M., Bon, C. et al. (2000). Collagen, convulxin, and thrombin stimulate aggregation-independent tyrosine phosphorylation of CD31 in platelets. Evidence for the involvement of Src family kinases. *J Biol Chem, 275*, 27339-47. ↗

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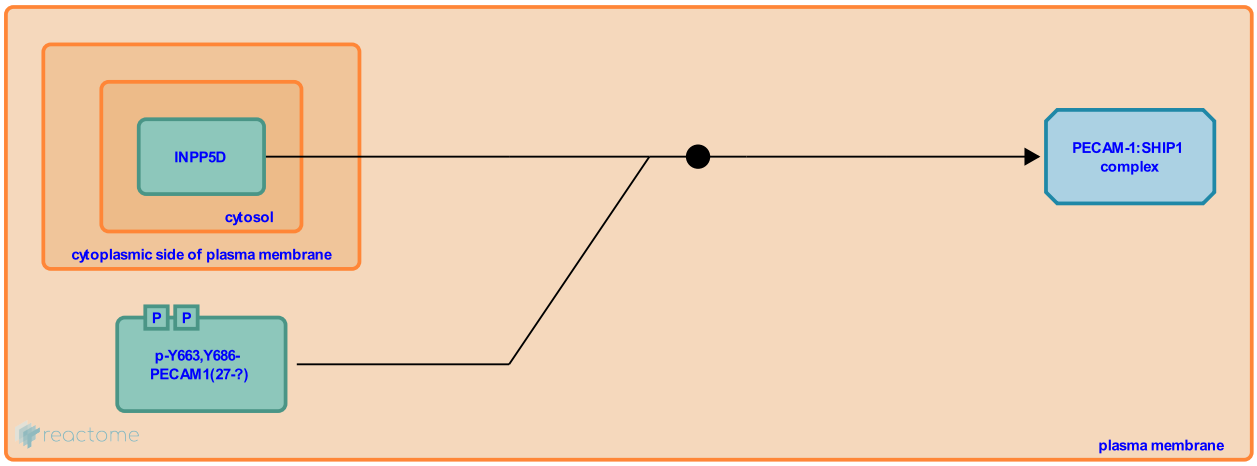
Interaction of PECAM-1 and SHIP ↗

Location: PECAM1 interactions

Stable identifier: R-HSA-210290

Type: binding

Compartments: plasma membrane, cytosol



PECAM/CD31 is a member of the immunoglobulin superfamily (IgSF) and has been implicated to mediate the adhesion and trans-endothelial migration of T-lymphocytes into the vascular wall, T cell activation and angiogenesis. It has six Ig homology domains within its extracellularly and an ITIM motif within its cytoplasmic region.
PECAM-mediated adhesion is complex, because it is capable of binding both to itself (homophilic adhesion) and to non-PECAM ligands (heterophilic adhesion). The trans-homophilic interaction between the two PECAM-1 molecules is mediated by their NH2-terminal membrane distal Ig homology domains 1 and 2 plus the proper spacing formed by the six Ig-homology domains.

Preceded by: Phosphorylation of PECAM-1 by Fyn or Lyn or c-Src

Literature references

Pumphrey, NJ., Buckley, CD., Douglas, MR., Taylor, V., Lord, JM., Salmon, M. et al. (1999). Differential association of cytoplasmic signalling molecules SHP-1, SHP-2, SHIP and phospholipase C-gamma1 with PECAM-1/CD31. *FEBS Lett, 450*, 77-83. ↗

Editions

2008-02-26	Authored	de Bono, B., Garapati, P V.
2008-02-26	Reviewed	Trowsdale, J.

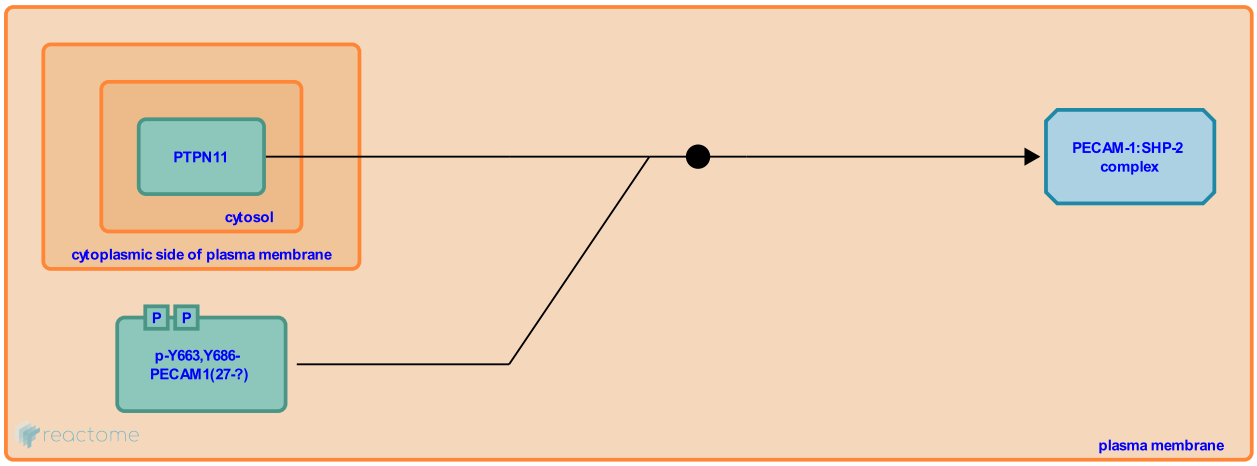
Interaction of PECAM-1 and SHP-2 ↗

Location: PECAM1 interactions

Stable identifier: R-HSA-210294

Type: binding

Compartments: plasma membrane, cytosol



PECAM-1 becomes tyrosine-phosphorylated during the platelet aggregation process; the phosphorylation of two tandem tyrosine residues (Y663 and Y686) within the cytoplasmic domain is required for downstream signalling events. Phosphorylation creates docking sites for the protein-tyrosine phosphatase SHP-2. The interaction between SHP-2 and PECAM-1 is dependent upon integrin-mediated platelet/platelet interactions and occurs via the Src homology 2 (SH2) domains of the phosphatase and highly conserved phosphatase-binding motifs encompassing phosphotyrosines 663 and 686 within the cytoplasmic domain of PECAM-1.

Preceded by: Phosphorylation of PECAM-1 by Fyn or Lyn or c-Src

Literature references

Ward, CM., Wang, R., Newman, PJ., Jackson, DE. (1997). The protein-tyrosine phosphatase SHP-2 binds platelet/endothelial cell adhesion molecule-1 (PECAM-1) and forms a distinct signaling complex during platelet aggregation. Evidence for a mechanistic link between PECAM-1- and integrin-mediated cellular signaling. *J Biol Chem, 272*, 6986-93. ↗

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2008-02-26	Authored	de Bono, B., Garapati, P V.
2008-02-26	Reviewed	Trowsdale, J.

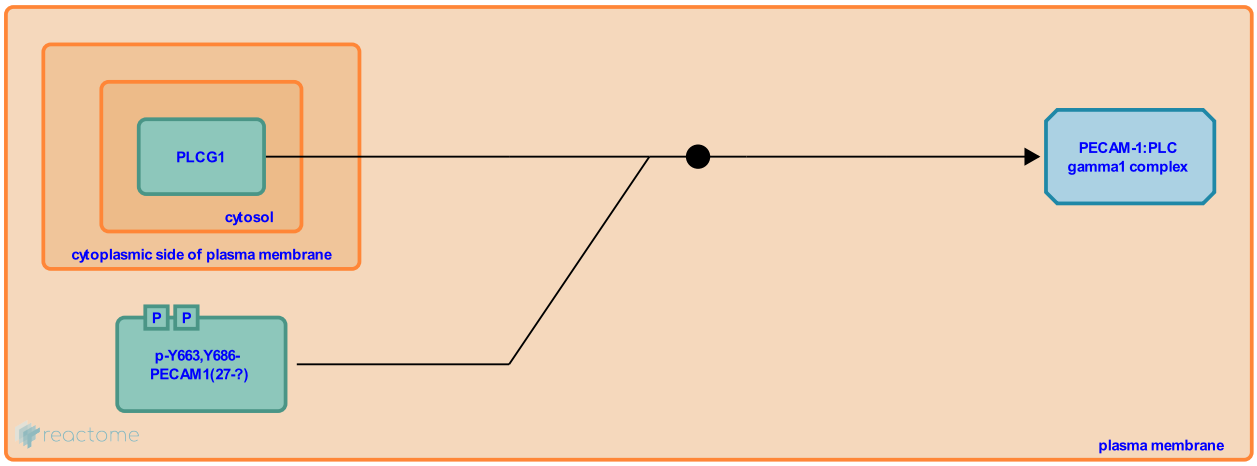
Interaction of PECAM-1 and PLC gamma1 ↗

Location: PECAM1 interactions

Stable identifier: R-HSA-210283

Type: binding

Compartments: plasma membrane, cytosol



Like SHP-1 and SHP-2, PLC-gamma 1 also interacts with PECAM-1. PLC-gamma 1 binds with both the tyrosine residues (Y663 and Y686). Unlike the N-SH2 domain, the C-SH2 domain on PLC-gamma 1 can only bind phosphotyrosine 663. The engagement of PECAM-1 with PLC-gamma 1 may lead to PLC-gamma 1 activation and subsequent calcium influx.

Preceded by: Phosphorylation of PECAM-1 by Fyn or Lyn or c-Src

Literature references

Pumphrey, NJ., Buckley, CD., Douglas, MR., Taylor, V., Lord, JM., Salmon, M. et al. (1999). Differential association of cytoplasmic signalling molecules SHP-1, SHP-2, SHIP and phospholipase C-gamma1 with PECAM-1/CD31. *FEBS Lett, 450*, 77-83. ↗

Editions

2008-02-26	Authored	de Bono, B., Garapati, P V.
2008-02-26	Reviewed	Trowsdale, J.

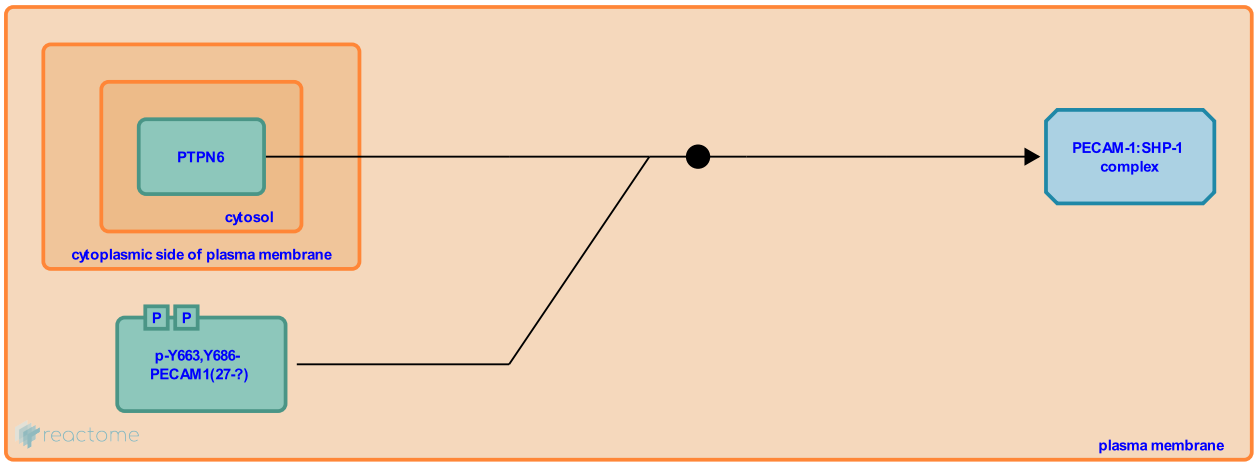
Interaction of PECAM-1 and SHP-1 ↗

Location: PECAM1 interactions

Stable identifier: R-HSA-210277

Type: binding

Compartments: plasma membrane, cytosol



The phosphorylation of two tandem tyrosine residues (Y663 and Y686) within the cytoplasmic domain of PECAM-1 is required for the downstream signalling events observed following PECAM-1 ligation. Both SH2 domains of SHP-1 are required in tandem to bind PECAM-1.

Preceded by: Phosphorylation of PECAM-1 by Fyn or Lyn or c-Src

Literature references

Gamble, JR., Hua, CT., Vadas, MA., Jackson, DE. (1998). Recruitment and activation of SHP-1 protein-tyrosine phosphatase by human platelet endothelial cell adhesion molecule-1 (PECAM-1). Identification of immunoreceptor tyrosine-based inhibitory motif-like binding motifs and substrates. *J Biol Chem, 273*, 28332-40. ↗

Editions

2008-02-26	Authored	de Bono, B., Garapati, P V.
2008-02-26	Reviewed	Trowsdale, J.

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