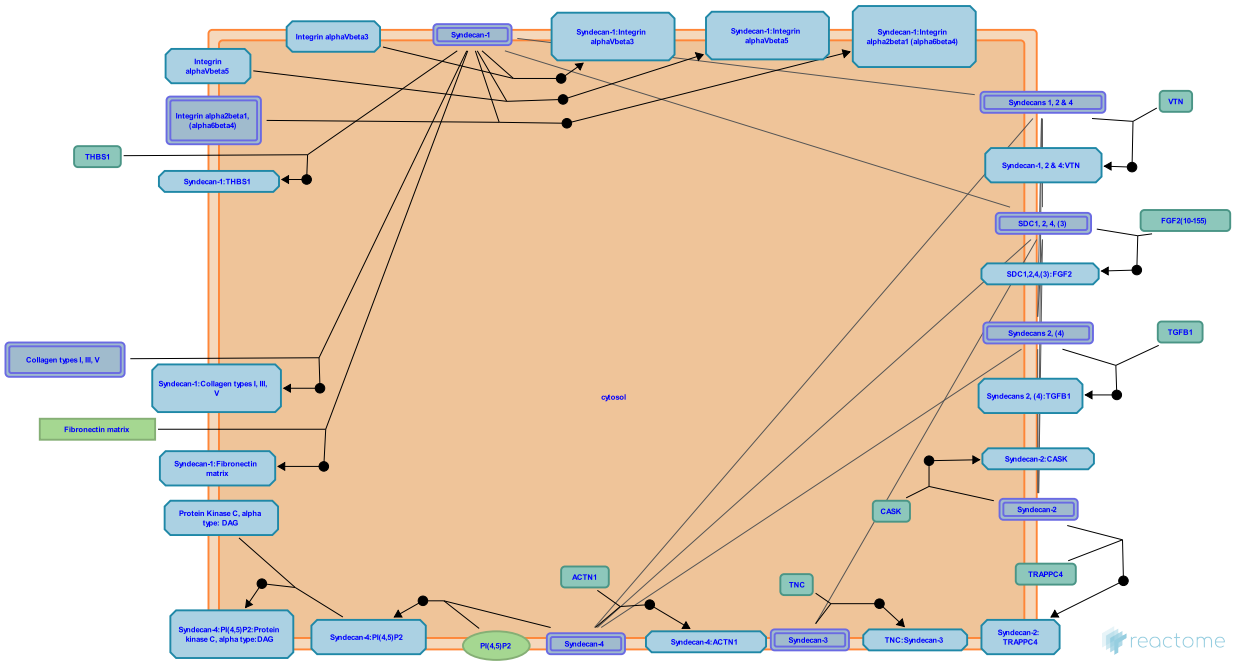
Syndecan interactions



Fuentes, J., Jupe, S., Ricard-Blum, S., Venkatesan, N.

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.

18/04/2024

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.

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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. ↗

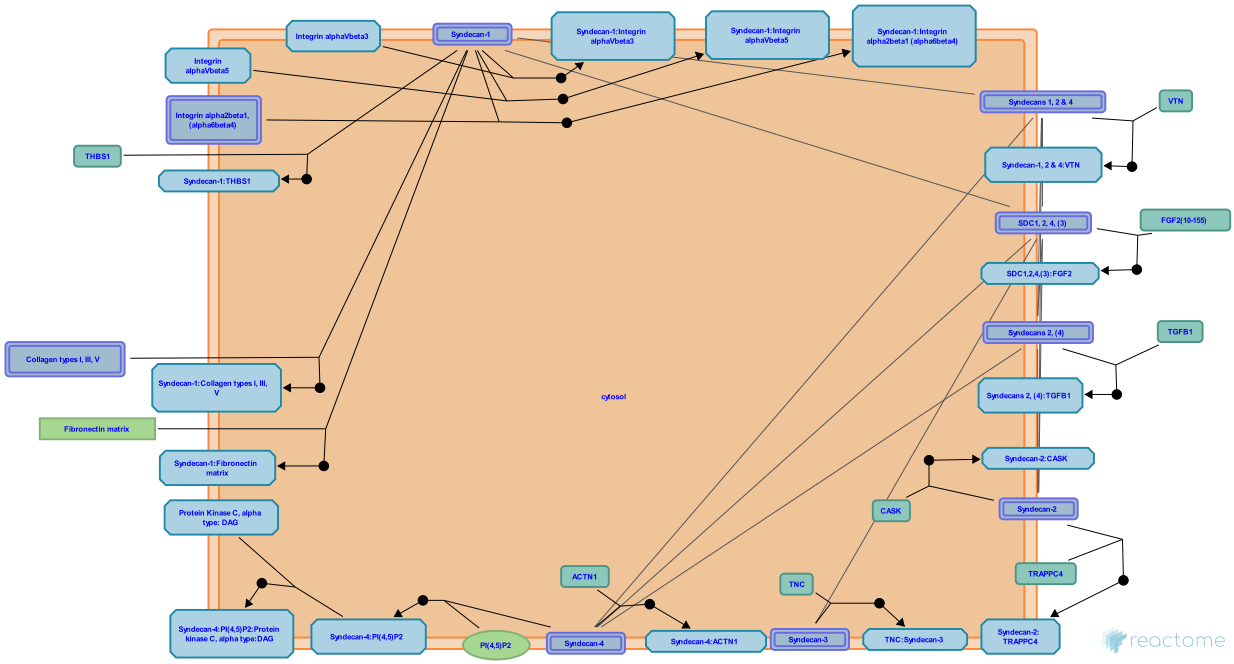
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Syndecan interactions ↗

Stable identifier: R-HSA-3000170



Syndecans are type I transmembrane proteins, with an N-terminal ectodomain that contains several consensus sequences for glycosaminoglycan (GAG) attachment and a short C-terminal cytoplasmic domain. Syndecan-1 and -3 GAG attachment sites occur in two distinct clusters, one near the N-terminus and the other near the membrane-attachment site, separated by a proline and threonine-rich 'spacer'. Syndecan ectodomain sequences are poorly conserved in the family and between species, but the transmembrane and cytoplasmic domains are highly conserved. Syndecan-1 and -3 form a subfamily. Syndecan core proteins form dimers (Choi et al. 2007) and at least syndecan-3 and -4 form oligomers (Asundi & Carey 1995, Shin et al. 2012). Syndecan-1 is the major syndecan of epithelial cells including vascular endothelium. Syndecan-2 is present mostly in mesenchymal, neuronal and smooth muscle cells. Syndecan-3 is the major syndecan of the nervous system, while syndecan-4 is ubiquitously expressed but at lower levels than the other syndecans (refs in Alexopoulou et al. 2007). The core syndecan protein has three to five heparan sulfate or chondroitin sulfate chains, which interact with a variety of ligands including fibroblast growth factors, vascular endothelial growth factor, transforming growth factor-beta, fibronectin, collagen, vitronectin and several integrins. Syndecans may act as integrin coreceptors. Interactions between fibronectin and syndecans are modulated by tenascin-C. Syndecans bind a wide variety of soluble and insoluble ligands, inckluding extracellular matrix components, cell adhesion molecules, growth factors, cytokines, and proteinases. As the cleaved ectodomains of syndecans retain the ability to bind ligands, ectodomain shedding is a mechanism for releasing soluble effectors that may compete for ligands with their cell-bound counterparts (Kainulainen et al. 1998). Shed ectodomains are found in inflammatory fluids (Subramanian et al. 1997) and may induce the proliferation of cancer cells (Maeda et al. 2004).

Literature references

Couchman, JR. (2010). Transmembrane signaling proteoglycans. *Annu. Rev. Cell Dev. Biol., 26*, 89-114. ↗

Couchman, JR., Alexopoulou, AN., Multhaupt, HA. (2007). Syndecans in wound healing, inflammation and vascular biology. *Int. J. Biochem. Cell Biol., 39*, 505-28. ↗

Rhodes, JM., Tkachenko, E., Simons, M. (2005). Syndecans: new kids on the signaling block. *Circ. Res., 96*, 488-500. ↗

Editions

2012-07-31	Authored	Jupe, S.
2013-04-26	Edited	Jupe, S.
2013-05-22	Reviewed	Ricard-Blum, S., Fuentes, J.

Syndecan-1 binds Integrin alphaVbeta3 ↗

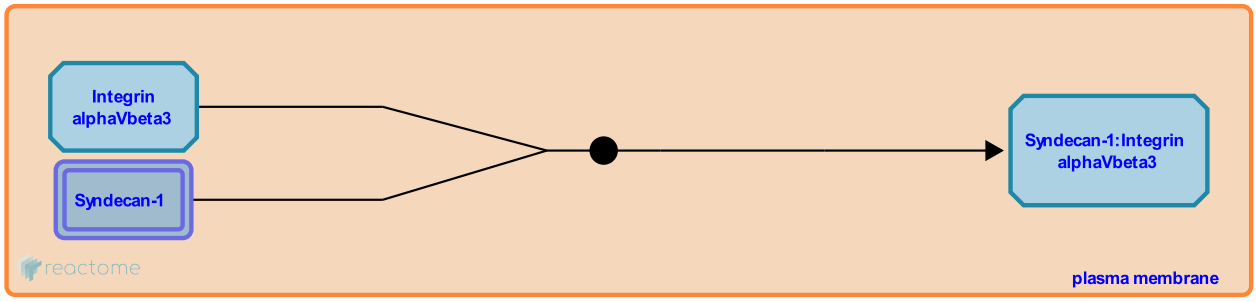
Location: Syndecan interactions

Stable identifier: R-HSA-2731123

Type: binding

Compartments: plasma membrane

Inferred from: Syndecan-1 binds integrin alphaVbeta3 (Homo sapiens)



Syndecans have attached heparan sulfate (HS) and to a lesser extent chondroitin sulfate (CS) chains. These allow interactions with a large number of proteins. Various enzymes involved in post-translational HS chain modifications produce unique binding motifs that selectively recognize different proteins (Tkachenko et al. 2005). It is thought that syndecans often act in concert with other receptors, e.g. alphavbeta3 and alphavbeta5 integrins cooperate with syndecan-1 during adhesion to vitronectin (Beauvais et al. 2004, McQuade et al. 2006). The relationship between syndecans and co-receptors is not well understood (Alexopoulou et al. 2007). Syndecan-null mice have subtle phenotypes when compared with mice deficient in HS chain synthesis or modification (Echtermeyer et al. 2001, Ishiquro et al. 2001, Götte et al. 2002).

Editions

2012-07-31	Authored	Jupe, S.
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Syndecan-1 binds Integrin alphaVBeta5 ↗

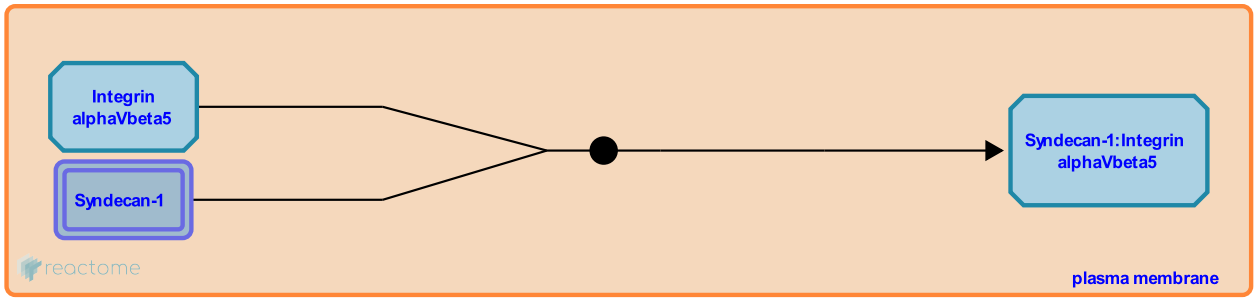
Location: Syndecan interactions

Stable identifier: R-HSA-2731081

Type: binding

Compartments: plasma membrane

Inferred from: Syndecan-1 binds integrin alphaVbeta5 (Homo sapiens)



Syndecans are type I transmembrane proteins, with an N-terminal ectodomain that contains several consensus sequences for glycosaminoglycan (GAG) attachment and a short C-terminal cytoplasmic domain. Syndecan-1 and -3 GAG attachment sites occur in two distinct clusters, one near the N-terminus and the other near the membrane-attachment site, separated by a proline and threonine-rich 'spacer'. Syndecan ectodomain sequences are poorly conserved in the family and between species, but the transmembrane and cytoplasmic domains are highly conserved. Syndecan-1 and -3 form a subfamily. Syndecan core proteins form dimers (Choi et al. 2007) and at least syndecan-3 and -4 form oligomers (Asundi & Carey 1995, Shin et al. 2012). Syndecan-1 is the major syndecan of epithelial cells including vascular endothelium. Syndecan-2 is present mostly in mesenchymal, neuronal and smooth muscle cells. Syndecan-3 is the major syndecan of the nervous system, while syndecan-4 is ubiquitously expressed but at lower levels than the other syndecans (refs in Alexopoulou et al. 2007).

Syndecans have attached heparan sulfate (HS) and to a lesser extent chondroitin sulfate (CS) chains. These allow interactions with a large number of proteins. Various enzymes involved in post-translational HS chain modifications produce unique binding motifs that selectively recognize different proteins (Tkachenko et al. 2005). It is thought that syndecans often act in concert with other receptors, e.g. integrins alphavbeta3 and alphavbeta5 cooperate with syndecan-1 during adhesion to vitronectin (Beauvais et al. 2004, McQuade et al. 2006). The relationship between syndecans and co-receptors is not well understood (Alexopoulou et al. 2007). Syndecan-null mice have subtle phenotypes when compared with mice deficient in HS chain synthesis or modification (Echtermeyer et al. 2001, Ishiquro et al. 2001, Götte et al. 2002). GPI-anchored glypicans and matrix HSPGs such as perlecan may compensate for the absence of syndecans.

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2012-07-31	Authored	Jupe, S.
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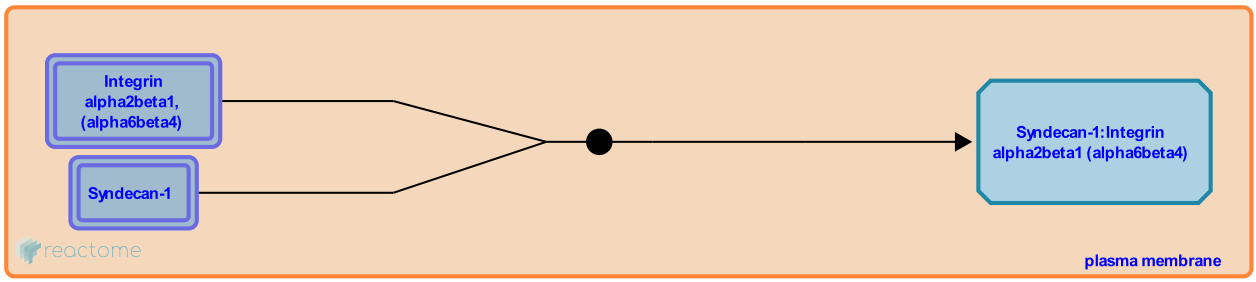
Syndecan-1 binds Integrins alpha2beta1, (alpha6beta4)

Location: Syndecan interactions

Stable identifier: R-HSA-2731074

Type: binding

Compartments: plasma membrane



Syndecans have attached heparan sulfate (HS) and to a lesser extent chondroitin sulfate (CS) chains. These allow interactions with a large number of proteins. Various enzymes involved in post-translational HS chain modifications produce unique binding motifs that selectively recognize different proteins (Tkachenko et al. 2005). It is thought that syndecans often act in concert with other receptors. Alpha2beta1 and alpha6beta4 integrins cooperate with syndecan-1 (SDC1) during adhesion to laminins (laminin alpha-1 Hozumi et al. 2006, laminin gamma-2, Ogawa et al. 2007, Wang et al. 2010). Interaction betweey SDC1 and alpha2beta1 integrin regulates cell adhesion to collagen (Vuoriluoto et al. 2008). SDC1 associates directly with the alphaVBeta3 and alphaVBeta5 integrins via its extracellular domain (Beauvais et al. 2004, McQuade et al. 2006). This association is required for integrin activation in a variety of carcinomas and probably reflects a generic role for the syndecan family as signaling 'hubs' at ECM adhesion sites (Fig. 1, Rapraeger 2013). The relationship between syndecans and co-receptors is not well understood (Alexopoulou et al. 2007). Syndecan-null mice have subtle phenotypes when compared with mice deficient in HS chain synthesis or modification (Echtermeyer et al. 2001, Ishiquro et al. 2001, Götte et al. 2002). GPI-anchored glypicans and matrix HSPGs such as perlecan may compensate for the absence of syndecans.

Literature references

Kariya, Y., Hashimoto, J., Miyazaki, K., Ogawa, T., Tsubota, Y. (2007). The short arm of laminin gamma2 chain of laminin-5 (laminin-332) binds syndecan-1 and regulates cellular adhesion and migration by suppressing phosphorylation of integrin beta4 chain. *Mol. Biol. Cell, 18*, 1621-33.

Nomizu, M., Yamada, Y., Hozumi, K., Nielsen, PK., Suzuki, N. (2006). Laminin alpha1 chain LG4 module promotes cell attachment through syndecans and cell spreading through integrin alpha2beta1. *J. Biol. Chem., 281*, 32929-40.

Rapraeger, AC., Beauvais, DM., Burbach, BJ. (2004). The syndecan-1 ectodomain regulates alphavbeta3 integrin activity in human mammary carcinoma cells. *J. Cell Biol., 167*, 171-81.

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2012-07-31	Authored	Jupe, S.
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Syndecan-1 binds THBS1 ↗

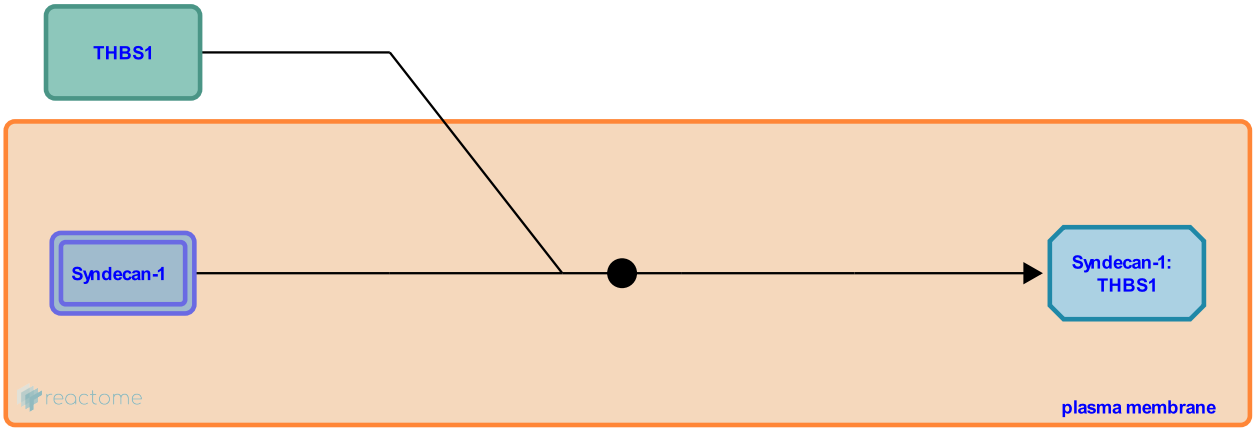
Location: Syndecan interactions

Stable identifier: R-HSA-2681675

Type: binding

Compartments: plasma membrane, extracellular region

Inferred from: Syndecan-1 binds THBS1 (Homo sapiens)



Syndecans have attached heparan sulfate (HS) and to a lesser extent chondroitin sulfate (CS) chains. These allow interactions with a large number of proteins, including heparin-binding growth factors such as fibroblast growth factors (Kiefer et al. 1990, Bernfield & Hooper 1991, Steinfeld et al. 1996), vascular endothelial growth factors (VEGFs) and transforming growth factor-Beta (Chen et al. 2000, Ishiguro et al. 2002). Various enzymes involved in post-translational HS chain modifications produce unique binding motifs that selectively recognize different proteins (Tkachenko et al. 2005). HS chains facilitate interactions of syndecan-1 with extracellular matrix proteins, including thrombospondin-1 (Sun et al. 1989, Lebakken & Rapraeger 1996, Adams et al. 2001, Yoneda & Couchman 2003). Syndecan-null mice have subtle phenotypes when compared with mice deficient in HS chain synthesis or modification (Echtermeyer et al. 2001, Ishiquro et al. 2001, Götte et al. 2002). GPI-anchored glypicans and matrix HSPGs such as perlecan may compensate for the absence of syndecans.

Editions

2012-07-31	Authored	Jupe, S.
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Syndecan-1 binds collagen types I, III, V ↗

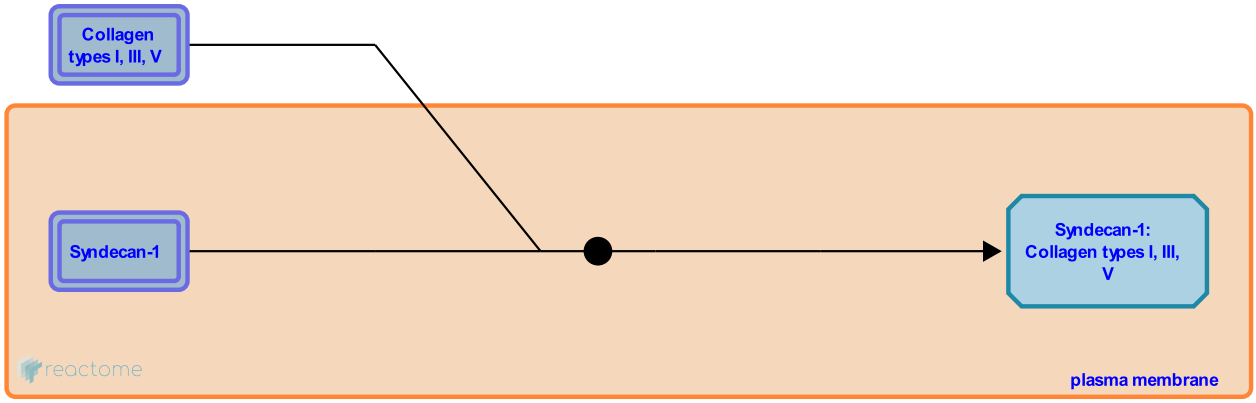
Location: Syndecan interactions

Stable identifier: R-HSA-2731075

Type: binding

Compartments: plasma membrane, extracellular region

Inferred from: Syndecan-1 binds collagen types I, III, V (Gallus gallus)



Syndecans have attached heparan sulfate (HS) and to a lesser extent chondroitin sulfate (CS) chains. These allow interactions with a large number of proteins. Various enzymes involved in post-translational HS chain modifications produce unique binding motifs that selectively recognize different proteins (Tkachenko et al. 2005). HS chains facilitate interactions of syndecan-1 with extracellular matrix proteins, including several types of collagen (type I, III and V - Koda et al. 1985). It is thought that syndecans often act in concert with other receptors, e.g. alphavbeta3 and alphavbeta5 integrins cooperate with syndecan-1 during adhesion to vitronectin (Beauvais et al. 2004, McQuade et al. 2006) while alpha2beta1 and alpha6beta4 integrins cooperate with syndecans during adhesion to laminin (laminin alpha-1 Hozumi et al. 2006, laminin gamma-2, Ogawa et al. 2007). Similarly syndecan-1 appears to support integrin alpha2Beta1-mediated adhesion to collagen (human to cow collagen I - Vuoriluoto et al. 2008). This relationship between syndecans and co-receptors is not well understood (Alexopoulou et al. 2007). Syndecan-null mice have subtle phenotypes when compared with mice deficient in HS chain synthesis or modification (Echtermeyer et al. 2001, Ishiquro et al. 2001, Götte et al. 2002).

Editions

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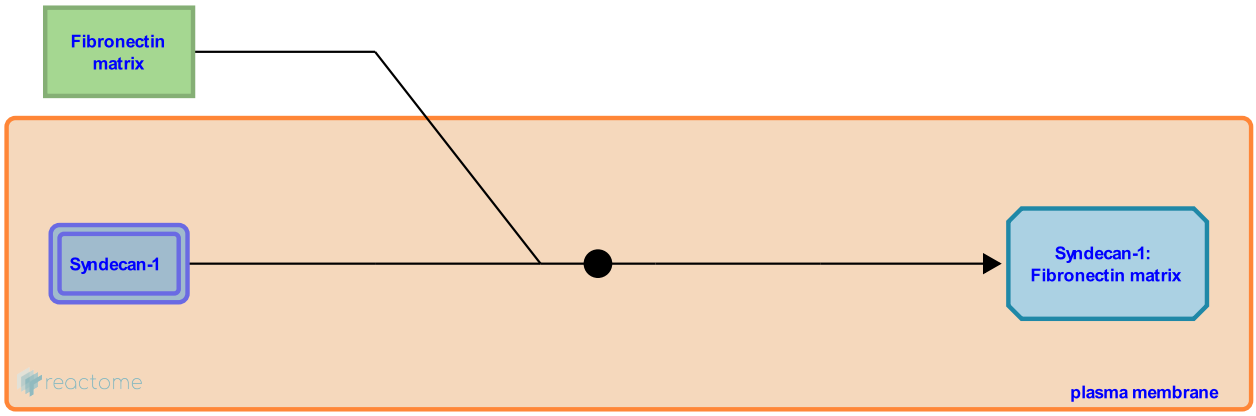
Syndecan-1 binds fibronectin ↗

Location: Syndecan interactions

Stable identifier: R-HSA-2731141

Type: binding

Compartments: plasma membrane, extracellular region



Syndecans have attached heparan sulfate (HS) and to a lesser extent chondroitin sulfate (CS) chains. These allow interactions with a large number of proteins. Various enzymes involved in post-translational HS chain modifications produce unique binding motifs that selectively recognize different proteins (Tkachenko et al. 2005). Syndecans binds with extracellular matrix proteins, including fibronectin (Human syndecan-1, Saunders & Bernfield 1988; rat syndecan-4 in Woods et al. 2000; rat syndecan-2 to bovine fibronectin in Klass & Woods 2000). Syndecan-1 functions to regulate integrin activity and fibronectin fibril assembly (Stepp et al. 2010).

Literature references

Saunders, S., Bernfield, M. (1988). Cell surface proteoglycan binds mouse mammary epithelial cells to fibronectin and behaves as a receptor for interstitial matrix. *J. Cell Biol., 106*, 423-30. ↗

Editions

2012-07-31	Authored	Jupe, S.
2013-04-26	Edited	Jupe, S.
2013-05-22	Reviewed	Fuentes, J.

Syndecan-2 binds CASK ↗

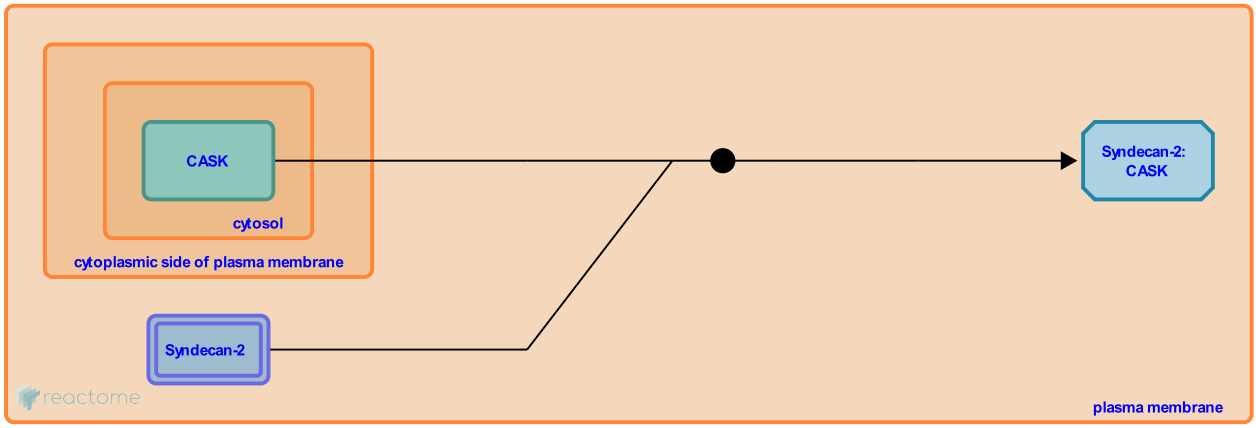
Location: Syndecan interactions

Stable identifier: R-HSA-2750181

Type: binding

Compartments: plasma membrane, cytosol

Inferred from: Syndecan-2 binds Cask (Rattus norvegicus)



Syndecans have attached heparan sulfate (HS) and to a lesser extent chondroitin sulfate (CS) chains. These allow interactions with a large number of proteins. Various enzymes involved in post-translational HS chain modifications produce unique binding motifs that selectively recognize different proteins (Tkachenko et al. 2005). Syndecan-null mice have subtle phenotypes when compared with mice deficient in HS chain synthesis or modification (Echtermeyer et al. 2001, Ishiquro et al. 2001, Götte et al. 2002). GPI-anchored glypicans and matrix HSPGs such as perlecan may compensate for the absence of syndecans.

Syndecans are also signalling molecules, interacting with cytoplasmic proteins. Syndecan-2 binds the kinase Ca2+/calmodulin associated serine/threonine kinase (CASK), a membrane-associated guanylate kinase (MAGUK) associated with intercellular junctions (Hsueh et al. 1998).

Editions

2012-07-31	Authored	Jupe, S.
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Syndecan-2 binds TRAPPC4 ↗

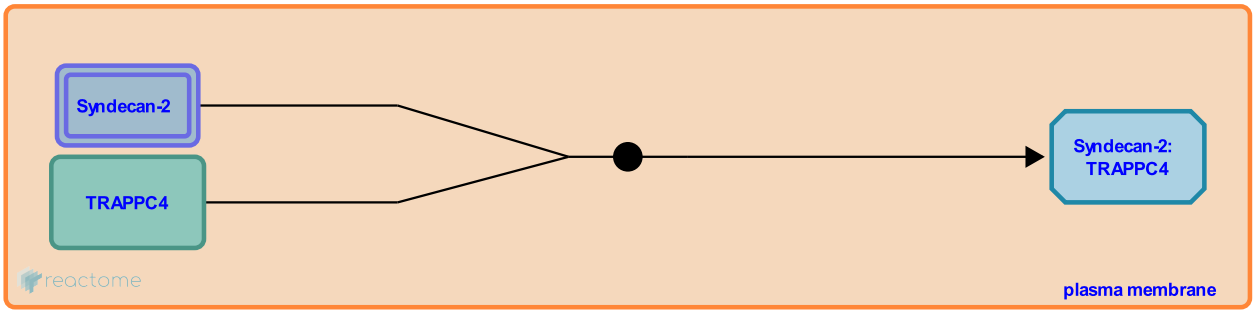
Location: Syndecan interactions

Stable identifier: R-HSA-2750177

Type: binding

Compartments: plasma membrane

Inferred from: Syndecan-2 binds Trappc4 (Mus musculus)



Syndecans have attached heparan sulfate (HS) and to a lesser extent chondroitin sulfate (CS) chains. These allow interactions with a large number of proteins. Various enzymes involved in post-translational HS chain modifications produce unique binding motifs that selectively recognize different proteins (Tkachenko et al. 2005). Syndecan-null mice have subtle phenotypes when compared with mice deficient in HS chain synthesis or modification (Echtermeyer et al. 2001, Ishiquro et al. 2001, Götte et al. 2002). GPI-anchored glypicans and matrix HSPGs such as perlecan may compensate for the absence of syndecans.

Syndecans are also signalling molecules, interacting with cytoplasmic proteins. Syndecan-2 binds Trafficking protein particle complex subunit 4 (TRAPPC4), also known as synbindin. It appears to be involved with postsynaptic membrane trafficking (Ethell et al. 2000). Syndecan-2 expression promotes dendritic spine maturation in neurons, and requires the C2 domain (Ethell et al. 2000), suggesting that syndecan-2 and synbindin recruit intracellular vesicles to postsynaptic sites. More recently TRAPPC4 was shown to be a component of the Transport Protein Particle, involved in endoplasmic reticulum-to-Golgi transport (Fan et al. 2009).

Editions

2012-07-31	Authored	Jupe, S.
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Syndecan-4 binds ACTN1 ↗

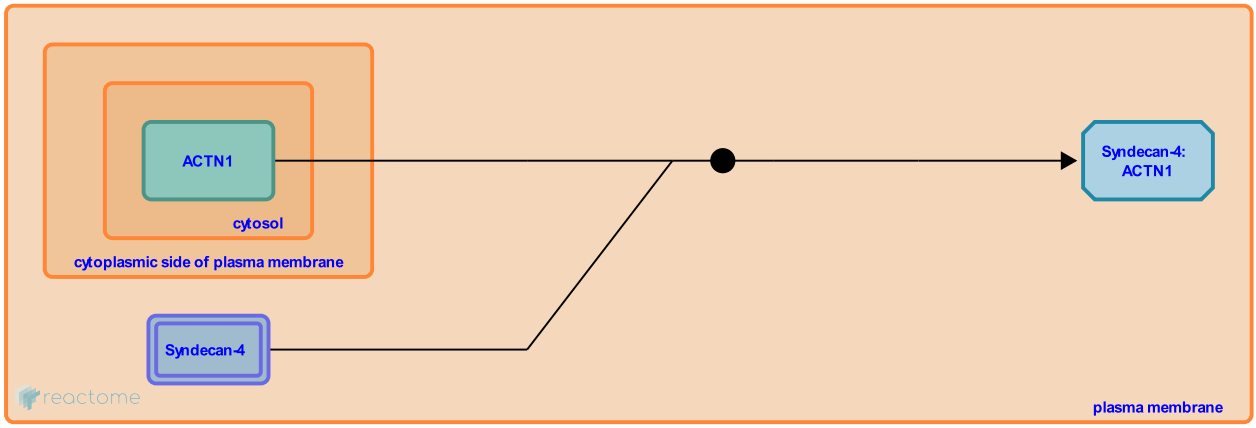
Location: Syndecan interactions

Stable identifier: R-HSA-2731149

Type: binding

Compartments: plasma membrane, cytosol

Inferred from: Syndecan-4 binds Actn1 (Rattus norvegicus)



Syndecans have attached heparan sulfate (HS) and to a lesser extent chondroitin sulfate (CS) chains. These allow interactions with a large number of proteins. Various enzymes involved in post-translational HS chain modifications produce unique binding motifs that selectively recognize different proteins (Tkachenko et al. 2005). Syndecan-null mice have subtle phenotypes when compared with mice deficient in HS chain synthesis or modification (Echtermeyer et al. 2001, Ishiquro et al. 2001, Götte et al. 2002). GPI-anchored glypicans and matrix HSPGs such as perlecan may compensate for the absence of syndecans. Syndecans are also signalling molecules, interacting with cytoplasmic proteins. Most of the work done has involved syndecan-4 (Multhaupt et al. 2009). The V-region of syndecan-4 interacts with the actin-bundling protein alpha-actinin (Greene et al. 2003, Choi et al. 2008, Shin et al. 2012), a direct link to the cell cytoskeleton.

Editions

2012-07-31	Authored	Jupe, S.
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2013-05-22	Reviewed	Fuentes, J.

Syndecan-4 binds PI(4,5)P2 ↗

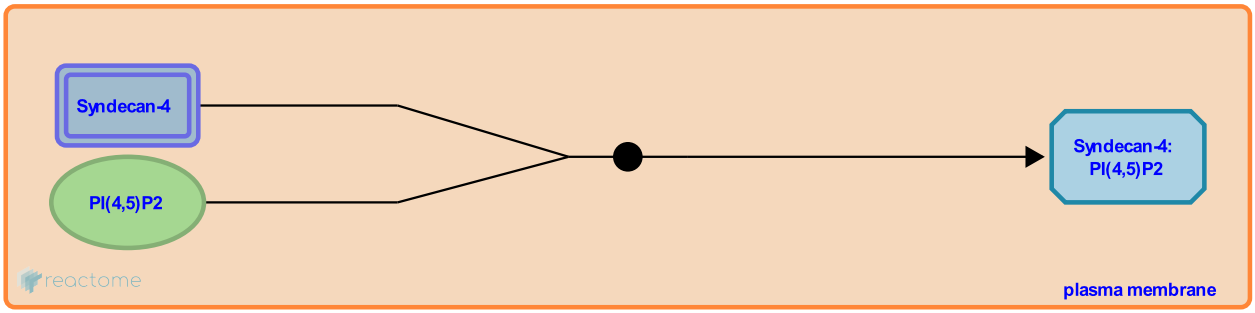
Location: Syndecan interactions

Stable identifier: R-HSA-2731147

Type: binding

Compartments: plasma membrane

Inferred from: Syndecan-4 binds PI(4,5)P2 (Danio rerio)



Syndecans have attached heparan sulfate (HS) and to a lesser extent chondroitin sulfate (CS) chains. These allow interactions with a large number of proteins. Syndecans are also signalling molecules, interacting with cytoplasmic proteins. Most studies have involved syndecan-4 (Multhaupt et al. 2009). Zebrafish and murine syndecan-4 V regions bind the membrane lipid phosphatidylinositol 4,5-bisphosphate (PI(4,5)P2) undergoing a shape change revealed by NMR spectroscopy (Oh et al. 1998, Whiteford et al. 2008). The resulting complex is able to bind protein kinase C alpha which is persistently activated in the absence of Ca2+ (Oh et al. 1997, Lee et al. 1998, Keum et al. 2004).

Followed by: Syndecan-4:PI(4,5)P2 binds PKC alpha:DAG

Editions

2012-07-31	Authored	Jupe, S.
2013-04-26	Edited	Jupe, S.
2013-05-22	Reviewed	Fuentes, J.

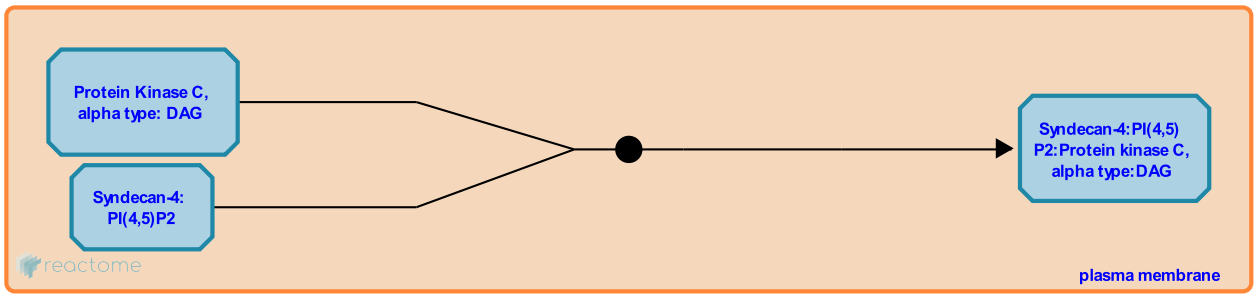
Syndecan-4:PI(4,5)P2 binds PKC alpha:DAG ↗

Location: Syndecan interactions

Stable identifier: R-HSA-2750187

Type: binding

Compartments: plasma membrane



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Syndecans are also signalling molecules, interacting with cytoplasmic proteins. Most of the work done has involved syndecan-4 (Multhaupt et al. 2009). Zebrafish and murine syndecan-4 V regions bind the membrane lipid phosphatidylinositol 4,5-bisphosphate (PI(4,5)P2) undergoing a shape change revealed by NMR spectroscopy (Oh et al. 1998, Whiteford et al. 2008). The resulting complex is able to bind protein kinase C alpha which is persistently activated in the absence of Ca2+ (Oh et al. 1997, Lee et al. 1998, Keum et al. 2004).

Preceded by: Syndecan-4 binds PI(4,5)P2

Literature references

Couchman, JR., Oh, ES., Woods, A. (1997). Multimerization of the cytoplasmic domain of syndecan-4 is required for its ability to activate protein kinase C. *J. Biol. Chem., 272*, 11805-11. ↗

Editions

2012-07-31	Authored	Jupe, S.
2013-04-26	Edited	Jupe, S.
2013-05-22	Reviewed	Fuentes, J.

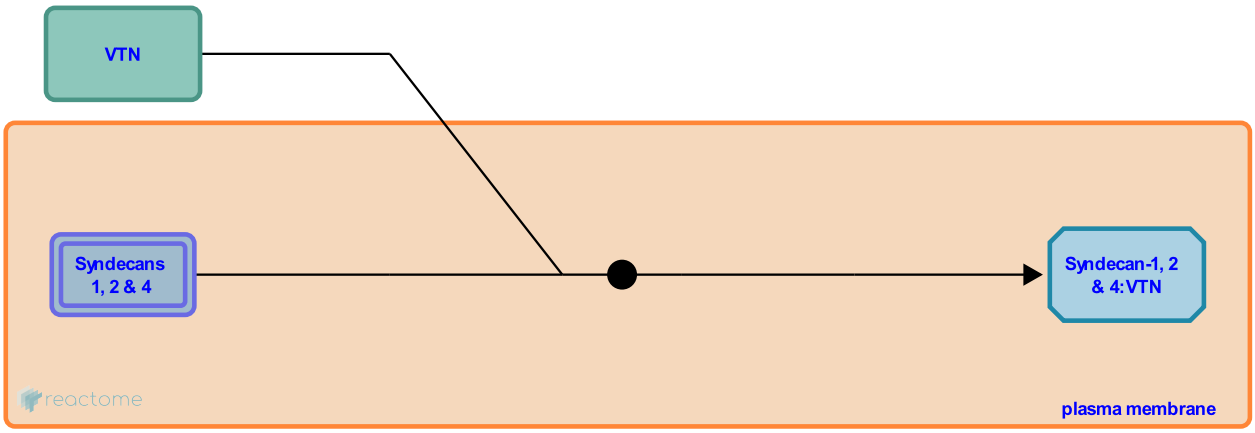
Syndecans 1, 2 & 4 bind VTN ↗

Location: Syndecan interactions

Stable identifier: R-HSA-2731122

Type: binding

Compartments: plasma membrane, extracellular region



Syndecans have attached heparan sulfate (HS) and to a lesser extent chondroitin sulfate (CS) chains. These allow interactions with a large number of proteins, including vitronectin (VTN) (Wilkins-Port & McKeown-Longo 1996, Wilkins-Port et al. 2003). It is thought that syndecans often act in concert with other receptors, e.g. integrins alphavbeta3 and alphavbeta5 cooperate with syndecan-1 during adhesion to vitronectin (Beauvais et al. 2004, McQuade et al. 2006) while alpha2beta1 and alpha6beta4 integrins cooperate with syndecans during adhesion to laminin (laminin alpha-1 Hozumi et al. 2006, laminin gamma-2, Ogawa et al. 2007). This relationship between syndecans and co-receptors is not well understood (Alexopoulou et al. 2007). Syndecan-null mice have subtle phenotypes when compared with mice deficient in HS chain synthesis or modification (Echtermeyer et al. 2001, Ishiquro et al. 2001, Götte et al. 2002). GPI-anchored glypicans and matrix HSPGs such as perlecan may compensate for the absence of syndecans.

Literature references

McKeown-Longo, PJ., Tominna-Sebald, E., Wilkins-Port, CE., Sanderson, RD. (2003). Vitronectin's basic domain is a syndecan ligand which functions in trans to regulate vitronectin turnover. *Cell Commun. Adhes., 10,* 85-103. ↗

Editions

2012-07-31	Authored	Jupe, S.
2013-04-26	Edited	Jupe, S.
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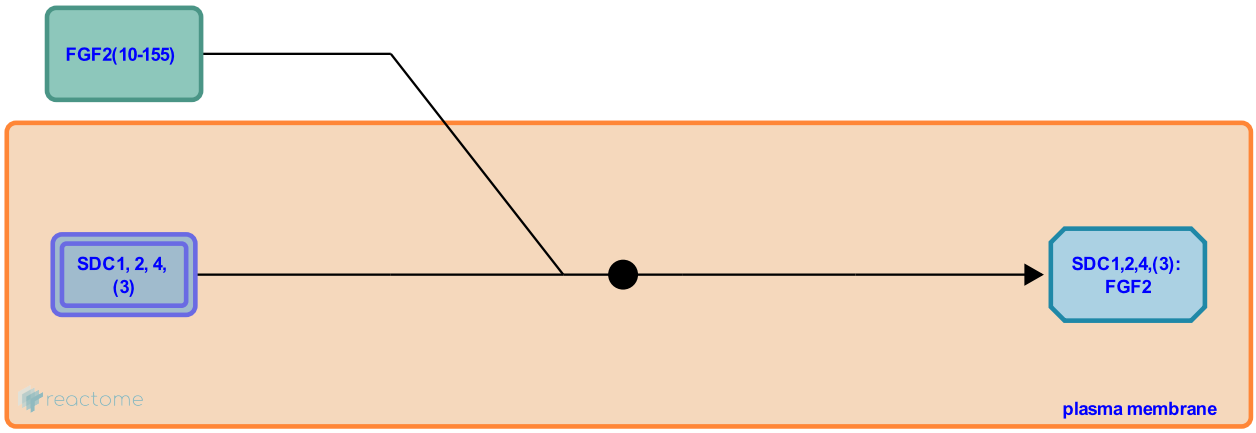
Syndecans 1, 2, 4, (3) bind FGF2 ↗

Location: Syndecan interactions

Stable identifier: R-HSA-2684507

Type: binding

Compartments: plasma membrane, extracellular region



Syndecans have attached heparan sulfate (HS) and to a lesser extent chondroitin sulfate (CS) chains. These allow interactions with a large number of proteins, including heparin-binding growth factors such as fibroblast growth factors (FGFs), mediating interaction with FGF receptors (Kiefer et al. 1990, Bernfield & Hooper 1991, Steinfeld et al. 1996, Chua et al. 2004). Various enzymes involved in post-translational HS chain modifications produce unique binding motifs that selectively recognize different proteins (Tkachenko et al. 2005).

Literature references

Van den Berghe, H., David, G., Steinfeld, R. (1996). Stimulation of fibroblast growth factor receptor-1 occupancy and signaling by cell surface-associated syndecans and glypican. *J. Cell Biol., 133,* 405-16. ↗

Editions

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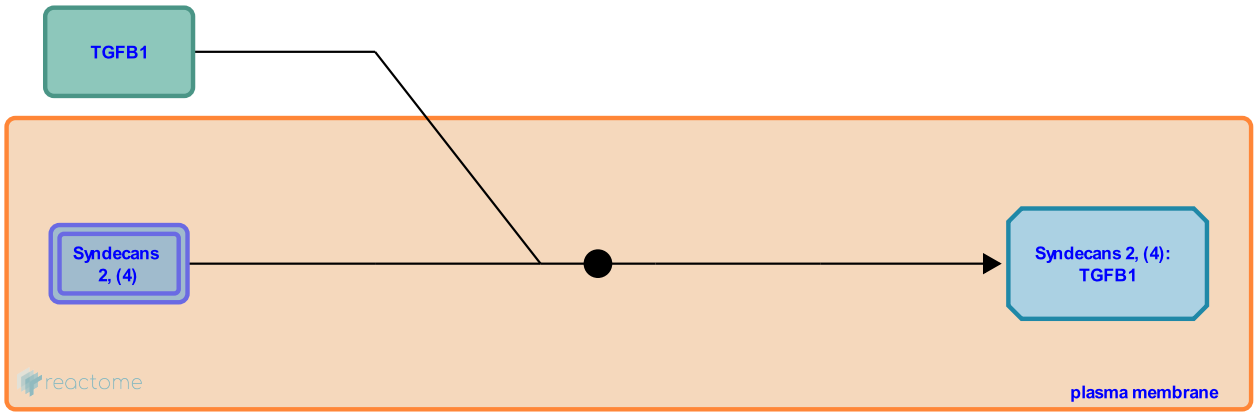
Syndecans 2, (4) bind TGFB1 ↗

Location: Syndecan interactions

Stable identifier: R-HSA-2731078

Type: binding

Compartments: plasma membrane, extracellular region



Syndecans have attached heparan sulfate (HS) and to a lesser extent chondroitin sulfate (CS) chains. These allow interactions with a large number of proteins, including transforming growth factor-Beta (Chen et al. 2000, Ishiguro et al. 2002). Various enzymes involved in post-translational HS chain modifications produce unique binding motifs that selectively recognize different proteins (Tkachenko et al. 2005). HS chains facilitate interactions of syndecan-1 with extracellular matrix proteins, including fibronectin (Saunders & Bemfield 1988, Woods et al. 2000), vitronectin, several types of collagen (type I, III and V Koda et al. 1985), and thrombospondin-1 (Sun et al. 1989, Yoneda & Couchman 2003). It is thought that syndecans often act in concert with other receptors, e.g. alphavbeta3 and alphavbeta5 integrins cooperate with syndecan-1 during adhesion to vitronectin (Beauvais et al. 2004, McQuade et al. 2006) while alpha2beta1 and alpha6beta4 integrins cooperate with syndecans during adhesion to laminin (laminin alpha-1 Hozumi et al. 2006, laminin gamma-2, Ogawa et al. 2007). The relationship between syndecans and co-receptors is not well understood (Alexopoulou et al. 2007). Syndecan-null mice have subtle phenotypes when compared with mice deficient in HS chain synthesis or modification (Echtermeyer et al. 2001, Ishiquro et al. 2001, Götte et al. 2002). GPI-anchored glypicans and matrix HSPGs such as perlecan may compensate for the absence of syndecans. Syndecans are also signalling molecules, interacting with cytoplasmic proteins. Most of the work done has involved syndecan-4 (Multhaupt et al. 2009). Zebrafish and murine syndecan-4 V regions bind the membrane lipid phosphatidylinositol 4,5 bisphosphate (PtdIns4,5P2) undergoing a shape change revealed by NMR spectroscopy (Whiteford et al. 2008). The resulting complex is able to bind protein kinase C alpha which is persistently activated in the absence of Ca2+ (Oh et al. 1997, Lee et al. 1998, Keum et al. 2004). Syndecan-2 binds the kinase Ca2+/calmodulin associated serine/threonine kinase (CASK), a membrane-associated guanylate kinase (MAGUK) associated with intercellular junctions (Hsueh et al. 1998). Trafficking protein particle complex subunit 4 (TRAPPC4) is a syndecan-2 interacting protein also known as synbindin. It appears to be involved with postsynaptic membrane trafficking (Ethell et al. 2000). Syndecan-2 expression promotes dendritic spine maturation in neurons, and requires the C2 domain (Ethell et al. 2000), suggesting that syndecan-2 and synbindin recruit intracellular vesicles to postsynaptic sites. More recently TRAPPC4 was shown to be a component of the Transport Protein Particle, involved in endoplasmic reticulum-to-Golgi transport (Fan et al. 2009). The V-region of syndecan-4 interacts with the actin-bundling protein alpha-actinin (Greene et al. 2003, Choi et al. 2008, Shin et al. 2012), a direct link to the cell cytoskeleton.

Literature references

Woods, A., Chen, L., Klass, C. (2004). Syndecan-2 regulates transforming growth factor-beta signaling. *J. Biol. Chem., 279*, 15715-8. ↗

Muramatsu, T., Kojima, T., Ishiguro, K. (2002). Syndecan-4 as a molecule involved in defense mechanisms. *Glycoconj. J., 19*, 315-8. ↗

Editions

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TNC binds Syndecan-3 ↗

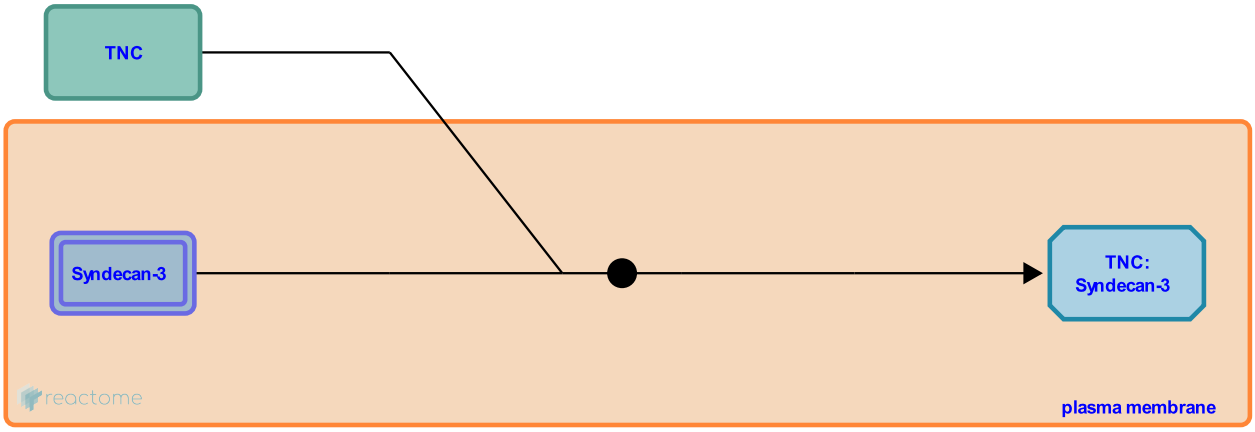
Location: Syndecan interactions

Stable identifier: R-HSA-2681694

Type: binding

Compartments: plasma membrane, extracellular region

Inferred from: Tnc binds sdc3 (Mus musculus)



Tenascins are a family of 4 oligomeric extracellular glycoproteins, tenascin (TN) C, R, X, and W. In rotary shadowing images TNC is seen as a symmetrical structure called a hexabrachion (Erickson & Iglesias 1984). This hexamer is formed from initial trimers (Kammerer et al. 1988). All members of the family are believed able to form trimers but only C, R and W have the extra cysteine required for form hexamers. All have amino-terminal heptad repeats, epidermal growth factor (EGF)-like repeats, fibronectin type III domain repeats, and a carboxyl-terminal fibrinogen-like globular domain (Hsia & Schwartzbauer 2005). TNC was the first of the family to be discovered and is the best characterised (Midwood et al. 2011). Its subunits vary greatly in size (between 190 and 330 kDa of the tenascin-C monomer) due to glycosylation and splicing isoforms (Joester & Faissner 1999). During embryonic development TNC is expressed in neural, skeletal, and vascular tissues. In adults it is detectable only in tendon and tissues undergoing remodeling processes such as wound repair and neovascularization, or in pathological processes such as inflammation and tumorigenesis. TNR forms dimers and trimers (Norenberg et al. 1992) and is expressed only in the developing and adult central nervous system. TNC and TNR-null mice (single and double knock-outs) have surprisingly normal gross phenotypes, but exhibit behavioural and wound healing abnormalities (Mackie & Tucker 1999, Montag-Sallaz & Montag 2003). TNX (termed tenascin-Y in chicken) is the largest member of the family and is widely expressed during development, but in adults is limited to musculoskeletal, cardiac, and dermal tissue. It can form trimers, though it lacks the amino-terminal cysteine residues involved in hexamer formation. It is clearly associated with a variant of a heritable connective tissue disorder known as Ehler-Danlos Syndrome, which is associated with fibrillar collagen defects (Burch et al. 1997, Mao et al. 2002). TNY is thought to be an avian orthologue of TNX (Chiquet-Ehrismann 2004). TNW, first identified in zebrafish (Weber et al. 1998), is the least well characterized member of the tenascin family. It forms trimers and is expressed in developing skeletal tissue, neural crest cells and kidney, a pattern that partially overlaps with TN-C.

TNC binds syndecan-3 (Salmivirta et al. 1991, Koyama et al. 1996) Syndecans are type I transmembrane proteins, with an N-terminal ectodomain that contains several consensus sequences for glycosaminoglycan attachment and a short C-terminal cytoplasmic domain. Syndecan-1 and -3 glycosaminoglycan attachment sites occur in two distinct clusters, one near the N-terminus and the other near the membrane-attachment site, separated by a proline and threonine-rich 'spacer'. Syndecan ectodomain sequences are poorly conserved in the family and between species, but the transmembrane and cytoplasmic domains are highly conserved. Syndecan-1 and -3 form a subfamily. Syndecan-3 on the cell surface is frequently oligomeric (Asundi & Carey 1995). Syndecans bind extracellular ligands via their attached heparan sulphate chains, playing roles in cell to matrix and cell to cell adhesion.

Editions

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