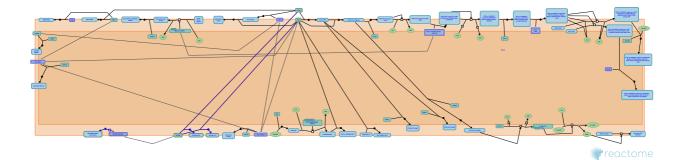


DSCAM interactions



Clemens, JC., Garapati, PV., Matthews, L.

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 <u>Creative Commons Attribution 4.0 International (CC BY 4.0)</u> <u>License</u>. For more information see our <u>license</u>.

This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the <u>Reactome Textbook</u>.

16/05/2024

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

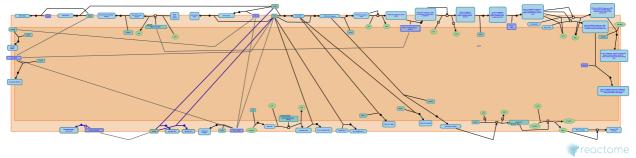
- Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18,* 142. 7
- Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics*, 33, 3461-3467. A
- 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. *オ*

This document contains 1 pathway and 3 reactions (see Table of Contents)

DSCAM interactions

Stable identifier: R-HSA-376172

Compartments: plasma membrane



DSCAM (Down syndrome cell adhesion molecule) is one of the members of the Ig superfamily CAMs with a domain architecture comprising 10 Ig domains, 6 fibronectin type III (FN) repeats, a single transmembrane and a C terminal cytoplasmic domain. DSCAM is implicated in Down syndrome (DS) due to the chromosomal location of the DSCAM gene, but no evidence supports a direct involvement of DSCAM with DS. It likely functions as a cell surface receptor mediating axon pathfinding. Besides these important implications, little is known about the physiological function or the molecular mechanism of DSCAM signal transduction in mammalian systems. A closely related DSCAM paralogue Down syndrome cell adhesion moleculelike protein 1 (DSCAML1) is present in humans. Both these proteins are involved in homophilic intercellular interactions.

Literature references

- Nikolaev, A., Ly, A., Stein, E., Zheng, Y., Tessier-Lavigne, M., Suresh, G. (2008). DSCAM is a netrin receptor that collaborates with DCC in mediating turning responses to netrin-1. *Cell*, 133, 1241-54.
- Agarwala, KL., Yamakawa, K., Tsutsumi, Y., Nakamura, S. (2000). Down syndrome cell adhesion molecule DSCAM mediates homophilic intercellular adhesion. *Brain Res Mol Brain Res, 79*, 118-26. *¬*

2010-01-05	Authored, Edited	Garapati, P V.
2010-08-10	Reviewed	Clemens, JC.
2024-03-05	Reviewed	Matthews, L.

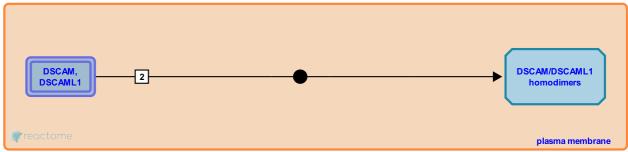
DSCAM/DSCAML1 homodimerization 7

Location: DSCAM interactions

Stable identifier: R-HSA-376122

Type: binding

Compartments: plasma membrane



DSCAM and DSCAML1 proteins are involved in homophilic intercellular interactions and these recognition events may play a role in neural connectivity. Recent studies in mouse demonstrate that DSCAM is selectively expressed in subclasses of cells and suggest that it uses homophilic repulsion to simultaneously promote both self avoidance (an essential developmental mechanism that allows axonal and dendrite processes to uniformly cover their synaptic fields) and tiling (ensures that the receptive fields of neurons from the same class do not overlap with one another) (Fuerst et al. 2008).

Literature references

- Burgess, RW., Masland, RH., Koizumi, A., Fuerst, PG. (2008). Neurite arborization and mosaic spacing in the mouse retina require DSCAM. *Nature, 451*, 470-4.
- Sanes, JR., Yamagata, M. (2008). Dscam and Sidekick proteins direct lamina-specific synaptic connections in vertebrate retina. *Nature, 451*, 465-9. 7
- Agarwala, KL., Yamakawa, K., Tsutsumi, Y., Nakamura, S. (2000). Down syndrome cell adhesion molecule DSCAM mediates homophilic intercellular adhesion. *Brain Res Mol Brain Res, 79*, 118-26. *¬*
- Ganesh, S., Agarwala, KL., Yamakawa, K., Amano, K., Suzuki, T., Tsutsumi, Y. (2001). Cloning and functional characterization of DSCAML1, a novel DSCAM-like cell adhesion molecule that mediates homophilic intercellular adhesion. *Biochem Biophys Res Commun, 285*, 760-72.

2010-01-05	Authored, Edited	Garapati, P V.
2010-08-10	Reviewed	Clemens, JC.

DSCAM binds DCC 7

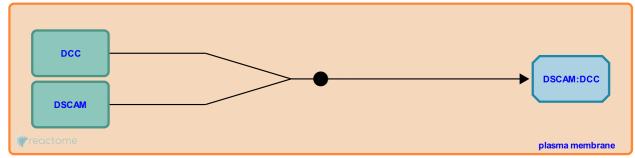
Location: DSCAM interactions

Stable identifier: R-HSA-451345

Type: binding

Compartments: plasma membrane

Inferred from: Dscam binds Dcc (Mus musculus)



DSCAM and DCC (Deleted in Colorectal Carcinoma) form a receptor complex in commissural axons in the absence of netrin1. They associate through a transmembrane interaction. The functional implication of this interaction is not known, but may allow DCC and DSCAM to contribute to other guidance pathways in a netrin1 independent fashion. It may serve as a way to hold DSCAM and DCC in a resting state, until netrin1 reaches a critical concentration at which both receptors are activated.

2010-01-05	Authored, Edited	Garapati, P V.
2010-08-10	Reviewed	Clemens, JC.

DSCAM binds Netrin-1 7

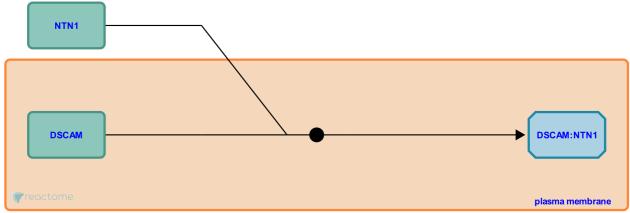
Location: DSCAM interactions

Stable identifier: R-HSA-376126

Type: binding

Compartments: plasma membrane, extracellular region

Inferred from: Dscam binds Netrin-1 (Mus musculus)



DSCAM binds netrin-1 and directs the turning of axons towards netrin-1 source independent of DCC or cooperatively depending on the cellular and developmental context. Signaling mechanisms activated by netrin-1 downstream of DSCAM involve phosphorylation of Fyn and PAK1.

2010-01-05	Authored, Edited	Garapati, P V.
2010-08-10	Reviewed	Clemens, JC.

Table of Contents

Introduction	1
The DSCAM interactions	2
➢ DSCAM/DSCAML1 homodimerization	3
➢ DSCAM binds DCC	4
➢ DSCAM binds Netrin-1	5
Table of Contents	6