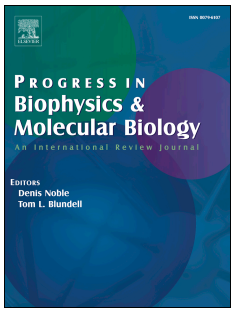
Accepted Manuscript



Signaling mechanism of the netrin-1 receptor DCC in axon guidance

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PII: S0079-6107(15)00046-2

DOI: 10.1016/j.pbiomolbio.2015.04.001

Reference: JPBM 1005

To appear in: *Progress in Biophysics and Molecular Biology*

Received Date: 26 January 2015

Revised Date: 26 March 2015

Accepted Date: 5 April 2015

Please cite this article as: Finci, L, Zhang, Y., Meijers, R, Wang, J.-H, Signaling mechanism of the netrin-1 receptor DCC in axon guidance, *Progress in Biophysics and Molecular Biology* (2015), doi: 10.1016/j.pbiomolbio.2015.04.001.

Signaling mechanism of the netrin-1 receptor DCC in axon guidance

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Abstract

DCC (Deleted in Colorectal Cancer) is a single-pass transmembrane protein that belongs to the immunoglobulin superfamily. It was originally identified as a prognostic tumor marker and then subsequently found to be a receptor for netrin-1. DCC plays a key role in axon guidance and also in a number of other important cellular processes. This review describes the current progress of the structural biology of DCC with an emphasis on how DCC is involved in the dual functionality of netrin-1 as a chemo-attractant as well as a repellent in axon guidance, referred to as bi-functionality. A perspective about other DCC ligands and the signaling mechanism of the cytoplasmic tail of DCC is also recapitulated.

Keywords: DCC, Netrin-1, Axon guidance, Structure, UNC5

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1. Introduction

DCC (Deleted in Colorectal Cancer) was initially identified as a prognostic tumor marker for colon cancer. It was characterized as a cell surface receptor encoded within a 370-kb region on chromosome 18q that is affected in tumors. The DCC gene was expressed in many normal tissues, but was absent in most colorectal carcinomas, hence the name DCC. Therefore at that early stage, DCC was proposed as a putative tumor suppressor gene (Fearon et al, 1990). Also expressed on spinal commissural axons, DCC was later established as a receptor for netrin-1, a neuronal axon guidance cue involved in determining the direction and extent of cell migration and axonal outgrowth in the developing nervous system (Chan et al, 1996; Keino-Masu et al, 1996).

During development, neuronal axons are guided along defined pathways by combined actions of attractive and repulsive cues in the extracellular environment. Diffusible chemoattractants attract axons to their targets, whereas repulsive guidance cues generate exclusion zones that axons avoid (Keynes & Cook, 1995; Tessier-Lavigne,