Netrins, a family of laminin-related molecules, have been proposed to act as guidance cues either during nervous system development or the establishment of the vascular system. This was clearly demonstrated for netrin-1 via its interaction with the receptors DCC and UNC5. Due to shared homologies with netrin-1, netrin-4 was also proposed to play a role in neuronal outgrowth and developmental/pathological angiogenesis via interactions with netrin-1 receptors. Here we present a 3.1 Å structure of netrin-4[1], which possesses unique features in comparison to previously crystallized netrin-1[2][3], and demonstrate that netrin-4 lacks the epitopes required to bind netrin-1 receptors. We show that netrin-4 disrupts laminin networks and basement membranes through high-affinity binding to the laminin γ1 chain, and hypothesize that this laminin-related function is essential for the previously described effects on axon growth promotion and angiogenesis.


**Keywords:** Extracellular Matrix, Axon and Dendritic Guidance