Molecular Characterization of Plexins: Signaling Mechanisms and Developmental Expression

Plexins are essential for proper neuronal migration during vertebrate development. Plexin A1 and Plexin A2 are transmembrane receptors that have been shown to transduce primarily repulsive signals from Semaphorins leading to growth cone collapse in migratory neurons.[1] Very little is known about the molecular mechanisms of these two pathways. Evidence of tyrosine phosphorylation of the cytoplasmic region of the Plexins has been shown and tyrosine kinases have been implicated in Plexin signaling, including the Src family kinase, Fyn.[2] Fyn activation is thought to be needed to phosphorylate proteins downstream responsible for inducting the growth cone collapse response.[3] How the binding of Semaphorins activates Fyn is still unknown. In order to understand the role Fyn might be playing in Plexin signaling, we investigated its role in phosphorylating Plexins at a highly conserved intracellular tyrosine phosphorylation site. The high conservation between vertebrate Plexin A1 and Plexin A2 orthologs made it plausible to propose similar hypotheses about both of the receptors: we hypothesize (1) that Fyn induces phosphorylation of Plexin A1 at Y1606 and of Plexin A2 at Y1605, and (2) that Fyn binds to the Plexin receptors upon the phosphorylation of the proposed sites. To determine the importance of this phosphorylation and the relative contribution of Fyn, we present here the establishment and characterization of a cell-based assay, as well as an *in vivo* model (*Danio rerio*).