

## Elucidation of PlexinA2 Signaling Mechanisms Critical for Zebrafish Eye Development

Marion E. Weir, Rachael L. Bassett, Kristen P. D'Elia, Bryan A. Ballif and Alicia M. Ebert

Department of Biology, University of Vermont, Burlington, VT, 05405, USA.

Neuronal migration in response to guidance cues is essential for proper patterning of the central nervous system. Semaphorins (Semas) are a class of guidance cues that have long been known to govern neuronal positioning. Recently we identified Sema6A-PlexinA2 (PlxnA2) signaling to be essential for proper development of the zebrafish eye. However, relatively little is known about the molecular mechanics of Sema-PlxnA signal transduction. Crystal structure studies suggest that Semas cluster PlxnA receptors. Furthermore, Sasaki *et al* (2002) showed that the Src family tyrosine kinase Fyn both phosphorylates and binds constitutively to PlxnA receptors. This leads to the hypothesis that Sema-dependent receptor clustering induces Fyn-dependent phosphorylation of PlxnA receptors which in turn effectuates PlxnA signal transduction. However, the specific Fyn-dependent PlxnA phosphorylation sites have yet to be identified. Using SILAC (Stable Isotope Labeling by Amino Acids in Cell Culture)-based quantitative mass spectrometry we have identified a novel PlxnA2 phosphorylation site induced by Fyn. The implications of this phosphorylation in Sema-PlxnA signaling, and its role in zebrafish eye development are discussed.