Functional analysis of Moe (Epb4.1l5) in zebrafish development and the identification of novel Epb4.1l5 binding proteins

Arne K Christensen, *University of Massachusetts Amherst*

Abstract

The zebrafish protein Mosaic eyes (Moe), and the mammalian orthologue Erythrocyte protein band 4.1-like 5 (Epb4.1l5), are FERM (for Protein 4.1, Ezrin, Radixin, Moesin) domain containing proteins that have important roles during embryonic development. Zebrafish with loss-of-function mutations in *moe* exhibit defects in retinal lamination, brain ventricle formation, and heart and body morphology. The mammalian *epb4.1l5* locus encodes at least two alternately spliced transcripts, the protein products (Epb4.1l5^{long} and Epb4.1l5^{short}) of each contain the FERM domain, but have unique C' termini. Mice with loss-of-function mutations in *epb4.1l5* have early developmental defects in germ layer morphogenesis during the Epithelial to Mesenchymal Transition (EMT), and these mutants fail to properly form a gut and neural tube. Our lab has shown that Moe functions in rod photoreceptors as a negative regulator of outer segment size, and directly binds to members of the Crumbs (Crb) family of proteins, which are apical polarity determinants. ^ Little is known of how Moe, or the Epb4.1l5 isoforms, perform their roles in cell or tissue morphogenesis. The collective aim of my studies was to elucidate the role of Moe and Epb4.1l5 isoforms in development and retinal function. I show that Moe and the apical polarity determinant Crb2a require reciprocal protein function for their respective localization at the eye and brain ventricle surface in zebrafish. I have identified multiple tissues and developmental stages wherein Moe and Crb proteins colocalize, and thus are likely to interact *in vivo*. I have identified specific sequences shared by Moe and Epb4.1l5 ^{long} that are important for function in specific tissues during zebrafish development, and I have investigated morphological, ultrastructural, and behavioral consequences of losing Moe (Epb4.1l5^{long}) function in the patterned zebrafish retina. I describe the interaction of Moe with the Ca^{2+} binding protein Calmodulin (CaM). I identify three novel binding partners of Epb4.1l5^{long}; Casein Kinase II, Moesin and Radixin, in mammalian retina and retinal pigmented epithelial (RPE) tissue homogenate. And lastly, I integrate the results of my studies to provide a model for Moe function, wherein Moe, together with Moesin and Radixin, link the vesicular transport Crb proteins to the actin cytoskeleton.^

Subject Area

Cellular biology

Recommended Citation