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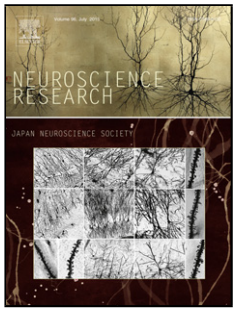

Title: Elavl3 regulates neuronal polarity through the alternative splicing of an embryo-specific exon in AnkyrinG

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Elavl3 regulates neuronal polarity through the alternative splicing of an embryo-specific exon in AnkyrinG

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Highlights

- Exon 34 of AnkyrinG is differentially spliced during development.
- Elavl3 protein promotes the exclusion of exon 34 of AnkyrinG.
- Exon 34 of AnkyrinG affects AnkyrinG localization and function.
- Exon 34 of AnkyrinG was acquired during vertebrate evolution.

Abstract

Alternative splicing of RNAs diversifies the functionalities of proteins, and it is optimized for each cell type and each developmental stage. nElavl (composed of Elavl2, Elavl3, and Elavl4) proteins are the RNA-binding proteins that is specifically expressed in neurons, regulate the alternative splicing of target RNAs, and promote neuronal differentiation and maturation. Recent studies revealed that *Elavl3* knockout (*Elavl3*$^{-/-}$) mice completely lost the expression of nElavl proteins in the Purkinje cells and exhibited cerebellar dysfunction. Here, we found that the alternative splicing of AnkyrinG exon 34 was misregulated in the cerebella of *Elavl3*$^{-/-}$ mice. AnkyrinG is an essential factor for the formation of neuronal polarity and is required for normal neuronal functions. We revealed that exon 34 of AnkyrinG was normally included in immature neurons and was mostly excluded in mature neurons; however, it was included in the cerebella of *Elavl3*$^{-/-}$ mice even in adulthood. In the Purkinje cells of adult *Elavl3*$^{-/-}$ mice, the length of the AnkyrinG-positive region shortened and somatic organelles leaked into the axons. These results suggested that exon 34 of AnkyrinG is an