

Splicing factor TRA2B is required for neural progenitor survival.

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Public Summary:

Alternative splicing of pre-mRNAs can rapidly regulate the expression of large groups of proteins. The RNA binding protein TRA2B (SFRS10) plays well-established roles in developmentally regulated alternative splicing during *Drosophila* sexual differentiation. TRA2B is also essential for mammalian embryogenesis and is implicated in numerous human diseases. Precise regulation of alternative splicing is critical to the development and function of the central nervous system; however the requirements for specific splicing factors in neurogenesis are poorly understood. In this study we focus on the role of TRA2B in mammalian brain development. We show that, during murine cortical neurogenesis, TRA2B is expressed in both neural progenitors and cortical projection neurons. Using cortex-specific *Tra2b* mutant mice, we find that TRA2B depletion results in apoptosis of the neural progenitor cells as well as disorganization of the cortical plate. Thus, TRA2B is essential for proper development of the cerebral cortex. The cut and paste process to generate genes regulates the production of proteins. One of the actors of the slicing is a molecule essential to the differentiation of sex in the fruit fly. This molecule is also essential for the development of the human in utero. This molecule expressed in the nerves is implicated in certain brain disease such as dementia or Parkinson. Thus, the cut and paste process of the genes is important to avoid nerve diseases but the mechanism by which the molecule of interest act is poorly understood. The research presented here shows that in a model such as the mouse, this molecule is expressed in nascent nerve and adult nerves. Erasing this molecule from the mouse brain leads to the death of the nascent nerves as well as disorganization of the cerebral cortex.

Scientific Abstract:

Alternative splicing of pre-mRNAs can rapidly regulate the expression of large groups of proteins. The RNA binding protein TRA2B (SFRS10) plays well-established roles in developmentally regulated alternative splicing during *Drosophila* sexual differentiation. TRA2B is also essential for mammalian embryogenesis and is implicated in numerous human diseases. Precise regulation of alternative splicing is critical to the development and function of the central nervous system; however, the requirements for specific splicing factors in neurogenesis are poorly understood. This study focuses on the role of TRA2B in mammalian brain development. We show that, during murine cortical neurogenesis, TRA2B is expressed in both neural progenitors and cortical projection neurons. Using cortex-specific *Tra2b* mutant mice, we show that TRA2B depletion results in apoptosis of the neural progenitor cells as well as disorganization of the cortical plate. Thus, TRA2B is essential for proper development of the cerebral cortex.

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