Invited Lecture

Structurally encoded functional switches in neuronal signalling

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During development of the brain cortex, young neurons migrate to form cortical layers with distinct functions. Teneurin (Ten), a cell adhesion molecule, plays an important role in this process. As a canonical cell adhesion molecule, it interacts in homophilic fashion to produce adhesion between cells. It also interacts with other proteins, especially Latrophilins (Lphn). The molecular determinants that underpin the interplay between these interactions is poorly understood. Our study presents cryo-electron microscopy data showing how Teneurins interact to produce cell adhesion. Structure-based mutagenesis coupled with cell binding and cell-based aggregation assays show that this interface is needed for effective trans homophilic interactions of Teneurin2 and 4. We bring our results from structural biology into the 'in vivo' model by expressing structure-based mutant Teneurins in developing mouse brains. The results suggest a robust structural switch underlies distinct functions of Teneurin in the developing brain.

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