A cytoplasmic motif targets neuroligin-1 exclusively to dendrites of cultured hippocampal neurons

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The formation of neuronal synapses is thought to depend on trans-synaptic interactions between cell adhesion molecules (CAMs) on the surface of axons and dendrites. Synapses are highly asymmetric structures. Pre- and post-synaptic domains might therefore be assembled around heterophilic CAMs which are polarized to axons vs. dendrites. We here investigated the targeting of neuroligin (NLG)-1, a heterophilic CAM, which promotes synapse formation through interaction with its receptor beta-neurexin in axons. We demonstrate that NLG-1 is highly polarized to the dendritic plasma membrane. Dendritic targeting relies on a cytoplasmic amino acid motif. By expressing chimeras of NLG-1 and CD8, an unpolarized protein, we show that the cytoplasmic domain of NLG-1 is necessary and sufficient for dendritic targeting. Furthermore, by truncation analysis we isolated a 32-amino-acid targeting motif. When appended to CD8 this cytoplasmic sequence is sufficient to direct exclusively dendritic localization of the protein. Analysis of yellow fluorescent protein-tagged NLG-1 revealed that vesicular structures containing NLG-1 are excluded from the axon indicating that polarized distribution may be achieved by direct dendritic transport. We propose that the strict polarity of NLG-1 contributes to the directional assembly of synapses during development of the central nervous system.

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