Synaptogenesis

Synaptogenesis is the formation of synapses between neurons in the nervous system. Although it occurs throughout a healthy person's lifespan, an explosion of synapse formation occurs during early brain development, known as exuberant synaptogenesis.

Synaptogenesis is particularly important during an individual's critical period, during which there is a certain degree of synaptic pruning due to competition for neural growth factors by neurons and synapses. Processes that are not used, or inhibited during their critical period will fail to develop normally later on in life.

Using Caenorhabditis elegans as a model, Shi et al. uncover that a Wnt-endocrine signaling pathway in the gut regulates synaptic development in the brain. A canonical Wnt signaling pathway promotes synapse formation by regulating the expression of the neuropeptides encoding gene nlp-40 in the gut, which functions through the neuronally expressed GPCR/AEX-2 receptor during development. Wnt-NLP-40-AEX-2 signaling likely acts to modulate neuronal activity. The study revealed a genetic role of the gut in synaptogenesis and identifies a novel contribution of the gut-brain axis [1)]

The mechanisms underlying neuronal development and synaptic formation in the brain depend on intricate cellular and molecular processes. The neuronal membrane glycoprotein GPM6a promotes neurite elongation, filopodia/spine formation, and synapse development, yet its molecular mechanisms remain unknown. Since the extracellular domains of GPM6a (ECs) command its function, Gutiérrez Fuster et al. investigated the interaction between ICAM5, the neuronal member of the intercellular adhesion molecule (ICAM) family, and GPM6a's ECs.

A study aimed to explore the functional relationship between GPM6a and ICAM5 in hippocampal culture neurons and cell lines. Immunostaining of 15 days in vitro (DIV) neurons revealed significant co-localization between endogenous GPM6a clusters and ICAM5 clusters in the dendritic shaft. These results were further corroborated by overexpressing GPM6a and ICAM5 in N2a cells and hippocampal neurons at 5 DIV. Moreover, results from the co-immunoprecipitations and cell aggregation assays prove the cis and trans interaction between both proteins in GPM6a/ICAM5 overexpressing HEK293 cells. Additionally, GPM6a and ICAM5 overexpression additively enhanced neurite length, the number of neurites in N2a cells, and filopodia formation in 5 DIV neurons, indicating their cooperative role. These findings highlight the dynamic association between GPM6a and ICAM5 during neuronal development, offering insights into their contributions to neurite outgrowth, filopodia formation, and cell-cell interactions [2)]

1)
Shi Y, Qin L, Wu M, Zheng J, Xie T, Shao Z. Gut neuroendocrine signaling regulates synaptic assembly in C. elegans. EMBO Rep. 2022 Jun 24:e53267. doi: 10.15252/embr.202153267. Epub ahead of print. PMID: 35748387.

2)
Gutiérrez Fuster R, León A, Aparicio GI, Brizuela Sotelo F, Scorticati C. Combined additive effects of neuronal membrane glycoprotein GPM6a and the intercellular cell adhesion molecule ICAM5 on neuronal morphogenesis. J Neurochem. 2024 Oct 1. doi: 10.1111/jnc.16231. Epub ahead of print. PMID: 39352694.